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- **SCARSELLI, Maria**
I-53100 Siena (IT)
- **PETRACCA, Roberto**
I-53100 Siena (IT)
- **BIANCONI, Irene**
I-20132 Milano (IT)
- **BRAGONZI, Alessandra**
I-20312 Milano (IT)
- **ALCALA' FRANCO, Beatriz**
I-20132 Milano (IT)

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(71) Applicants:

- **GlaxoSmithKline Biologicals S.A.**
1330 Rixensart (BE)
- **Ospedale San Raffaele S.r.l.**
20132 Milano (IT)

(74) Representative: **Carpmaels & Ransford LLP**
One Southampton Row
London WC1B 5HA (GB)

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(72) Inventors:

- **MASIGNANI, Vega**
I-53100 Siena (IT)

(54) **PSEUDOMONAS ANTIGENS AND ANTIGEN COMBINATIONS**

(57) An effective *Pseudomonas aeruginosa* vaccine may require one or several antigenic components, and so various antigens of *P. aeruginosa* are identified for use in immunisation. These polypeptides may optionally be used in combination with other nosocomial antigens.

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Description

[0001] This application claims the benefit of UK provisional application 1221638.8 filed November 30th, 2012, the complete contents of all of which are hereby incorporated herein by reference for all purposes.

TECHNICAL FIELD

[0002] This invention relates to antigens derived from *P. aeruginosa* and to their use in immunisation.

BACKGROUND ART

[0003] *Pseudomonas aeruginosa*, an opportunistic gram-negative bacterial pathogen found in most environments including water reservoirs and soil, is one of the leading nosocomial pathogen worldwide. This Gram-negative bacterium is best known for being the leading cause of morbidity and mortality in cystic fibrosis (CF) patients, with 80% of adult CF patients carrying *P. aeruginosa* in their lungs [1], and has recently gained notoriety by being classified as a 'superbug' by the media. The latter emanates from the intrinsic resistance that this opportunistic pathogen has against antibiotics [2], and its prominence as a cause of nosocomial infections (*i.e.* there are an estimated 10,000 cases each year in UK hospitals) [3].

[0004] Despite considerable advances in antimicrobial therapy, effective treatment and control of *P. aeruginosa* infections remains a persistent problem, primarily because of the natural resistance of the organism and its remarkable ability to acquire resistance to multiple antimicrobial agents by various mechanisms.

[0005] A vaccine against *P. aeruginosa* has long been sought after, but is so far not available. Several vaccine candidates have been assessed in experimental animals and humans, which include sub-cellular fractions, capsule components, purified and recombinant proteins.

[0006] Unique characteristics of the host and the pathogen have complicated the vaccine development.

[0007] Reference 4 reports a recombinant protein based vaccine approach on a single fusion polypeptide obtained by the fusion of two fragments of two outer membrane derived proteins, namely OprF and OprI. This vaccine is undergoing clinical trials [5], and further details are disclosed in ref. 6.

[0008] Thus there remains a need to identify further and improved antigens for use as single antigens or in combinations in *P. aeruginosa* vaccines, and in particular for vaccines which are useful against multiple *P. aeruginosa* pathologies, comprising e.g. cystic fibrosis. Summing up, there is still the need to obtain an effective vaccine against *P. aeruginosa*.

DISCLOSURE OF THE INVENTION

[0009] The inventors have identified various *P. aeruginosa* polypeptides that are useful for immunisation, either alone or in combination. These polypeptides may be combined with *P. aeruginosa* saccharides or other *P. aeruginosa* polypeptides or antigens derived from other pathogens (*i.e.* *S. aureus*, *E. coli*, etc). The antigens are useful in *P. aeruginosa* vaccines but may also be used as components in vaccines for immunising against multiple pathogens.

[0010] The inventors have identified in total the following polypeptides:

a PSE54 (PA5340) antigen; a PSE44-4 (PA3526) antigen; a PSE10-1 (PA1178) antigen; a PSE21-5 (PA5112) antigen; a PSE27-1 (PA0328) antigen; a PSE52-1 (PA4765) antigen; a PSE53-1 (PA5047) antigen; PSE11-3 (PA1248) antigen; a PSE41-5 (PA2407) antigen; a PSE47A-2 (PA4082); PSE5-1 (PA0595); PSE13-2 (PA1954); PSE17-1 (PA3692); PSE18-2 (PA4370); PSE20-1 (PA4735); PSE23-1 (PA3647); PSE24-1 (PA0126); PSE25-1 (PA0189); PSE26-1 (PA0274); PSE28-2 (PA0537); PSE31-2 (PA0737); PSE33-2 (PA1086); PSE42-1 (PA2793); PSE45-2 (PA3535); PSE50-1 (PA4578); PSE51-4 (PA4667); PSE19-1 (PA4710); PSE34-1 (PA1106); PSE36-3 (PA1324); PSE38-1 (PA1777).

[0011] Amongst the total set of selected antigens it can be distinguished a 'first antigen group' which is described as a group of antigens for which no prior attempts have been made to test them as vaccine antigens. The "first antigen group" comprises 25 out of the 30 selected antigens.

[0012] In particular the "first antigen group" comprises the following antigens: a PSE54 (PA5340) antigen; a PSE44-4 (PA3526) antigen; a PSE21-5 (PA5112) antigen; a PSE27-1 (PA0328) antigen; a PSE53-1 (PA5047) antigen; a PSE41-5 (PA2407) antigen; a PSE47A-2 (PA4082) antigen; a PSE5-1 (PA0595) antigen; a PSE13-2 (PA1954) antigen; a PSE17-1 (PA3692) antigen; a PSE18-2 (PA4370) antigen; a PSE20-1 (PA4735) antigen; a PSE23-1 (PA3647) antigen; a PSE24-1 (PA0126) antigen; a PSE25-1 (PA0189) antigen; a PSE26-1 (PA0274) antigen; a PSE28-2 (PA0537) antigen; a PSE31-2 (PA0737) antigen; a PSE33-2 (PA1086) antigen; a PSE42-1 (PA2793) antigen; a PSE45-2 (PA3535) antigen; a PSE50-1 (PA4578) antigen; a PSE51-4 (PA4667) antigen; a PSE34-1 (PA1106) antigen; and a PSE36-3 antigen (PA1324).

[0013] Thus the invention provides an immunogenic composition comprising one or more (i.e. 1, 2, 3, 4, 5 or more) antigens selected from the first antigen group.

[0014] Within the first antigen group, antigens are preferably selected from the list of a PSE54 (PA5340) antigen, PSE21-5 (PA5112) antigen; a PSE27-1 (PA0328) antigen; a PSE41-5 (PA2407) antigen; a PSE44-4 (PA3526) antigen;

a PSE47A-2 (PA4082) antigen; and/or a PSE53-1 (PA5047) antigen.

[0015] Within the 'first antigen group', antigens are preferably selected from a subset of 5 polypeptides, and particularly useful in producing a protective immunogenic response *in vivo* if used as single antigens or in combinations are: a PSE54 (PA5340) antigen; a PSE44-4 (PA3526) antigen; a PSE21-5 (PA5112) antigen; a PSE53-1 (PA5047) antigen; PSE42-1 (PA2793).

[0016] Within the first antigen group, all the listed antigens can be selected as single antigens for use against *P. aeruginosa*, with the proviso that the PSE27-1 (PA0328) antigen can be usefully omitted from this list ('first antigen group').

[0017] A "second antigen group" is defined as a group of identified antigens which has already been proposed as possible immunogenic stand-alone vaccine antigen but never considered in combination of at least two (ie. 2, 3, 4, 5, 6 or more) antigens in *in vivo* experiments. A subset of the "second antigen group" is defined as the "further antigenic polypeptides" group and comprises those antigenic polypeptides that have been extensively tested as vaccine antigens *in vivo*.

[0018] The second antigen group comprises the following list of antigens: PSE10-1 (PA1178) antigen; PSE11-3 (PA1248) antigen; PSE52-1 (PA4765) antigen; PSE19-1 (PA4710) antigen; and PSE38-1 (PA1777) antigen.

[0019] The subset of the second antigen group defined as "further antigenic polypeptides" group comprises the following list of antigens: PiiA (PA4524), OprF-OprI, FliC (PA1092), FliD (PA1094) and/or Exoprotein A (PA1148). Hence, the "second antigen group" comprises 10 polypeptides in total.

[0020] Thus the invention provides an immunogenic composition comprising a combination of antigens, said combination comprising two or more (i.e. 2, 3, 4, 5, 6 or more) antigens selected from the group consisting of: a PSE54 (PA5340) antigen; a PSE44-4 (PA3526) antigen; a PSE10-1 (PA1178) antigen; a PSE21-5 (PA5112) antigen; a PSE27-1 (PA0328) antigen; a PSE52-1 (PA4765) antigen; a PSE53-1 (PA5047) antigen; PSE11-3 (PA1248) antigen; a PSE41 (PA2407) antigen; a PSE47A-2 (PA4082); PSE5-1 (PA0595); PSE13-2 (PA1954); PSE17-1 (PA3692); PSE18-2 (PA4370); PSE20-1 (PA4735); PSE23-1 (PA3647); PSE24-1 (PA0126); PSE25-1 (PA0189); PSE26-1 (PA0274); PSE28-2 (PA0537); PSE31-2 (PA0737); PSE33-2 (PA1086); PSE42-1 (PA2793); PSE45-2 (PA3535); PSE50-1 (PA4578); PSE51-4 (PA4667); PSE19-1 (PA4710); PSE34-1 (PA1106); PSE36-3 (PA1324); PSE38-1 (PA1777).

[0021] Within the first antigen group, antigens are preferably selected from a subset of 7 of 30 polypeptides, namely: PSE54 (PA5340), PSE47A-2 (PA4082), PSE41-5 (PA2407), PSE53-1 (PA5047), PSE21-5 (PA5112), PSE27-1 (PA0328) or PSE44-4 (PA3526) antigens and a subset of the "second antigen group", namely: PSE52-1 (PA4765), PSE10-1 (PA1178), PSE11-3 (PA1248) and the OprF-OprI which is selected from the subset of the 'second antigen group' defined as "further antigenic polypeptides" group. Thus the invention provides an immunogenic composition comprising a combination of antigens, said combination comprising two or more (i.e. 2, 3, 4, 5, 6 or more) antigens selected from the group consisting of these eleven antigens.

[0022] Within the 11 antigens selected from the first, the second and the further antigenic polypeptides group there are 55 possible pairs of antigen combinations.

[0023] Within the 'second antigen group', comprising the subset of 5 polypeptides referred to herein as 'the further antigenic polypeptides', there are in total 10 polypeptides. The invention provides an immunogenic composition comprising a combination of antigens, said combination comprising a mixture of two or more (i.e. 2, 3, 4, 5, 6 or more) antigens selected from any of the preferred antigens of the "first antigen group" with anyone of the "second antigen group" or "further antigenic polypeptides" group.

[0024] The invention provides an immunogenic composition comprising a combination of antigens, said combination comprising a mixture of two or more (i.e. 2, 3, 4, 5, 6 or more) antigens selected from any antigens from the first antigen group and the second antigen group.

[0025] Within the 30 antigens of the mixture of the first antigen group and second antigen group there are 435 possible pairs of different antigens. All such pairs are disclosed herein and are part of the invention. Thus the invention provides an immunogenic composition comprising a pair of antigens, wherein said pair is one of said 435 pairs.

[0026] Within the 35 antigens of the mixture of the first antigen group and second antigen group there are 595 possible pairs of different antigens. All such pairs are disclosed herein and are part of the invention. Thus the invention provides an immunogenic composition comprising a pair of antigens, wherein said pair is one of said 595 pairs.

[0027] In one embodiment, a composition includes at least one antigen (i.e. 1, 2, 3, 4, 5, 6 or more) selected from the first antigen group and at least one antigen (i.e. 1, 2, 3, 4, 5, 6 or more) selected from the second antigen group. Antigens from the first antigen group may be selected from the preferred subset of PSE54 (PA5340), PSE47A-2 (PA4082), PSE41-5 (PA2407), PSE53-1 (PA5047), PSE21-5 (PA5112), or PSE44-4 (PA3526) antigens, and antigens from the second antigen group can be selected from PSE52-1 (PA4765), PSE10-1 (PA1178) or from any of the further antigenic polypeptide sub-set of the second antigen group, preferring the fusion OprF-OprI..

[0028] The invention also provides an immunogenic composition comprising a combination of antigens, said combination comprising two or more (*i.e.* 2, 3, 4 or 5) antigens selected from the group consisting of: (1) a PSE54 antigen; (2) a PSE10-1 antigen; (3) a PSE44-4 antigen; (4) a PSE52-1 antigen; (5) a PSE53-1 antigen; (6) a PSE21-5 antigen; (7) a PSE27-1 antigen; (8) a PSE47A-2 antigen; and/or (9) an OprF-OprI antigen.

[0029] Within the preferred 9 antigens selected from the first antigen group, the second antigen group and/or the further antigen group there are 36 possible pairs of different antigens. All such pairs are disclosed herein and are part of the invention. Thus the invention provides an immunogenic composition comprising a pair of antigens, wherein said pair is one of said 36 pairs.

[0030] The composition may also include an adjuvant *e.g.* an aluminium hydroxide adjuvant.

[0031] Advantageous combinations of the invention are those in which two or more antigens act synergistically. Thus the protection against *P. aeruginosa* disease achieved by their combined administration exceeds that expected by mere addition of their individual protective efficacy.

[0032] Specific combinations of interest include, but are not limited to:

- (1) An immunogenic composition comprising a PSE54 antigen, a PSE27 antigen
- (2) An immunogenic composition comprising a PSE54 antigen and OprF-OprI antigen
- (3) An immunogenic composition comprising a PSE54 antigen, a PSE27 antigen and/or a OprF-OprI antigen
- (4) An immunogenic composition comprising PSE54 antigen and/or a PSE44 antigen
- (5) An immunogenic composition comprising PSE54 antigen and/or PSE21-5 antigen
- (6) An immunogenic composition comprising PSE54 antigen and/or PSE52-1 antigen
- (7) An immunogenic composition comprising PSE47A-2 antigen and/or PSE53-1 antigen
- (8) An immunogenic composition comprising PSE54 antigen and/or PSE10-1 antigen
- (9) An immunogenic composition comprising PSE54 and PSE53-1 antigen
- (10) An immunogenic composition comprising PSE47A-2 and PSE52-1 antigen
- (11) An immunogenic composition comprising PSE54 antigen and/or PSE44-4 antigen and/or PSE47A-2 antigen
- (12) An immunogenic composition comprising a PSE47A-2 antigen, a PSE53-1 antigen, or a PSE54 antigen and/or a PSE27 antigen.
- (13) An immunogenic composition comprising (a) a PSE47A-2 antigen combined with a PSE53-1 antigen, or (b) a PSE54 antigen combined with a PSE21-5 antigen.
- (14) An immunogenic composition comprising a PSE47A-2 antigen and/or PSE52 antigen.

[0033] In some embodiments, any of these immunogenic and protective compositions may include additional pseudomonas antigens, and these further antigens can be polypeptides and/or saccharides. For example, they can useful also include one or more Pseudomonas antigens belonging to the "second antigen group" which includes the "further antigenic polypeptides" group, which include the fusion polypeptide OprF-OprI in a synergistic manner.

[0034] The immunogenic composition may also include an adjuvant.

Further polypeptide antigens group

[0035] In additions to antigens from the various antigen groups of the invention, immunogenic compositions may include one or more of the following *P. aeruginosa* antigens (or antigens comprising immunogenic fragment(s) thereof to enhance the efficacy against *P. aeruginosa* of an immune response elicited by the composition:

- OprF-OprI [4]
- PA4525, known also as PilA

- PA1092, known also as FliC
- PA1094, known also as FliD
- PA1148, Exoprotein A or Exotoxin A

5 **[0036]** The "further antigenic polypeptides" group is defined as a subgroup of the second antigen group. This group of known antigens can be useful used in combination with 1, 2 or more other useful antigens of the first antigen group or the second antigen group.

10 **Combinations with other *P. aeruginosa* derived antigens**

[0037] The individual antigens identified in the antigen groups of the invention may be used in combination with other antigens from *P. aeruginosa*. In some embodiments the other antigens from *P. aeruginosa* can be in the form of saccharides conjugated with a carrier protein. Thus the invention provides an immunogenic composition comprising a combination of:

- 15
- (1) one or more antigen(s) selected from the first, second, or further antigen groups (as defined above); and/or their combination or admixture and
 - (2) one or more conjugates of a saccharide moiety, and a carrier protein.

20 **[0038]** A conjugate used in component (2) of this combination includes a saccharide moiety and a carrier moiety.

[0039] In embodiments of the invention, the composition further comprises the *P. aeruginosa* 5-hexose Psl polysaccharide, which can be present as free polysaccharide and/or conjugated to a carrier protein. Optionally, one or more flagellin adjuvants and/or fusion proteins of the invention act as the carrier protein and have Psl polysaccharide conjugated thereto. For example, monomers and/or dimers of the *P. aeruginosa* polysaccharide can be conjugated to one or more

25 of the flagellin adjuvants and/or fusion proteins. See reference 7.

[0040] A conjugate used in component (2) of this combination includes a saccharide moiety and a carrier moiety. The saccharide moiety is from the exopolysaccharide of a *P. aeruginosa*. The saccharide may be a polysaccharide having the size that arises during purification from bacteria, or it may be an oligosaccharide achieved by fragmentation of such a polysaccharide.

30 **[0041]** The invention also provides an immunogenic composition comprising a combination of:

- (1) one or more antigen(s) selected from the first, second, or further antigen groups;
- (2) one or more conjugates of a *P. aeruginosa* exopolysaccharide and a carrier protein.

35 **[0042]** The carrier moiety in these conjugates will usually be a protein, but usually not one of the antigens of (1).

[0043] Typical carrier proteins are bacterial toxins, such as diphtheria or tetanus toxins, or toxoids or mutants or fragments thereof. The CRM197 diphtheria toxin mutant [8] is useful. Other suitable carrier proteins include the *N. meningitidis* outer membrane protein complex [9], synthetic peptides [10], heat shock proteins [11], pertussis proteins [12], cytokines [13], lymphokines [13], growth factors [13], artificial proteins comprising multiple human CD4⁺ T cell epitopes from various pathogen-derived antigens [14] such as N19 [15], protein D from *H. influenzae* 16, pneumolysin [17] or its non-toxic derivatives [18], pneumococcal surface protein PspA [19], iron-uptake proteins [20], toxin A or B from *C. difficile* [21], recombinant *P. aeruginosa* exoprotein A (rEPA) [22], etc. In some embodiments the carrier protein is a *P. aeruginosa* protein, such as an antigen selected from the first, second, or further antigen groups.

40 **[0044]** Where a composition includes more than one conjugate, each conjugate may use the same carrier protein or a different carrier protein.

[0045] Conjugates may have excess carrier (w/w) or excess saccharide (w/w). In some embodiments, a conjugate may include substantially equal weights of each.

[0046] The carrier molecule may be covalently conjugated to the carrier directly or via a linker. Direct linkages to the protein may be achieved by, for instance, reductive amination between the saccharide and the carrier, as described in, for example, references 23 and 24. The saccharide may first need to be activated e.g. by oxidation. Linkages via a linker group may be made using any known procedure, for example, the procedures described in references 25 and 26. A preferred type of linkage is an adipic acid linker, which may be formed by coupling a free -NH₂ group (e.g. introduced to a glucan by amination) with adipic acid (using, for example, diimide activation), and then coupling a protein to the resulting saccharide-adipic acid intermediate [27]. Another preferred type of linkage is a carbonyl linker, which may be formed by reaction of a free hydroxyl group of a saccharide CDI [28] followed by reaction with a protein to form a carbamate linkage. Other linkers include β-propionamido [29], nitrophenyl-ethylamine [30], haloacyl halides [31], glycosidic linkages [32], 6-aminocaproic acid [33], ADH [34], C₄ to C₁₂ moieties [35], etc. Carbodiimide condensation can also be used [36].

[0047] The individual antigens identified in the antigen groups of the invention may be used as carrier proteins for exopolysaccharides, to form a covalent conjugate. Thus the invention provides an immunogenic composition comprising a conjugate of (1) an antigen selected from the first, second, and further antigen groups and (2) a *P. aeruginosa* exopolysaccharide. These conjugates may be combined with any of the antigens disclosed herein.

Combinations with other pathogens derived (*non-pseudomonas*) antigens

[0048] The individual antigens identified in the antigen groups of the invention may be used also in combination with other pathogens derived antigens, *i.e.* non-pseudomonas antigens, and in particular with antigens from bacteria associated with nosocomial infections. Thus the invention provides an immunogenic composition comprising a combination of:

- (1) one or more antigen(s) selected from the first, second, and further antigen groups (as defined above); and
- (2) one or more antigen(s) selected from the pathogen group consisting of: *S. aureus* (including one or more conjugates of (i) a *S.aureus* exopolysaccharide; and/or one or more protein antigens of *S.aureus*); *Burkholderia cenocepacia* (*e.g.* O antigen lipopolysaccharide), *Clostridium difficile*; *Candida albicans*; and/or extraintestinal pathogenic *Escherichia coli*.

First antigen group

PA0328 or PSE27-1

[0049] The 'PA0328' antigen is annotated as 'outer membrane autotransporter'. In the PAO1 strain is annotated as 'hypothetical protein' and has amino acid sequence SEQ ID NO: 1 and described as PA0328 in reference 37. This sequence is annotated in NCBI as GI: 15595525. It has been recently demonstrated to be an autotransporter protein relevant in the virulence strategy adopted by *Pseudomonas aeruginosa* through its arginine-specific aminopeptidase activity, as in reference 38. Sometimes, PA0328 is referred to herein as 'PSE27-1' or as 'PSE27'.

[0050] Useful PA0328 antigens can elicit an antibody (*e.g.* when administered to a human) that recognises SEQ ID NO: 1 and/or may comprise an amino acid sequence: (a) having 50% or more identity (*e.g.* 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 1; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 1, wherein 'n' is 7 or more (*e.g.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PA0328 proteins include variants of SEQ ID NO: 1. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 1. Other preferred fragments lack one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (*e.g.* 1, 2,3,4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 27, 28, 29, 30, 35, 40, 45, 49, 50 or more) from the N-terminus of SEQ ID NO: 1 while retaining at least one epitope of SEQ ID NO: 1. The final 40-50 C-terminal amino acids of SEQ ID NO: 1 can usefully be omitted. The first 22 N-terminal amino acids of SEQ ID NO: 1 can usefully be omitted. Other fragments omit one or more protein domains.

[0051] SEQ ID NO: 36 is a useful fragment of SEQ ID NO: 1 ('PA0328₂₂₋₆₄₇'). This fragment omits the leader peptide at the N- terminal portion to enable expression and purification.

PA5112 or PSE21-5

[0052] The 'PSE21-5' antigen is annotated as 'Esterase or EstA' in the PAO1 strain. In the PAO1 strain PSE21-5 is described as 'PA5112' and has amino acid sequence SEQ ID NO: 3. In the PAO1 strain its identifier in NCBI is GI: 15600305 See Ref.37. Sometimes, PA5112 is referred to herein as 'PSE21-5' or 'PSE21'.

[0053] Useful PSE21-5 antigens can elicit an antibody (*e.g.* when administered to a human) that recognises SEQ ID NO: 3 and/or may comprise an amino acid sequence: (a) having 50% or more identity (*e.g.* 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 3; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 3, wherein 'n' is 7 or more (*e.g.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE21-5 proteins include variants of SEQ ID NO: 3. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 3. Other preferred fragments lack one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 3 while retaining at least one epitope of SEQ ID NO: 3. The final 40 C-terminal amino acids of SEQ ID NO: 3 can usefully be omitted. The first 24 N-terminal amino acids of SEQ ID NO: 3 can usefully be omitted. Other fragments omit one or more protein domains. PSE21-5 is naturally a long protein and so the use of fragments is helpful *e.g.* for purification, handling, fusion, expression, *etc.*

[0054] SEQ ID NO: 38 is a useful fragment of SEQ ID NO: 3 ('PSE21-5₂₅₋₆₄₆'). This fragment includes the most

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exposed domain of PSE21-5 and is more easily used at an industrial scale.

PA2407 or PSE41-5

5 [0055] The 'PSE41-5' antigen is annotated as 'probable adhesion protein'. In the PAO1 strain PSE41-5 is named PA2407 and has amino acid sequence SEQ ID NO: 5 (GI: 15597603). See Ref.37. Sometimes, PA2407 is referred to herein as 'PSE41-5' or 'PSE41'. Sometimes, PA2407 is referred to herein as 'PSE41-5' or 'PSE41'.

10 [0056] Useful 'PSE41-5' antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 5 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 5; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 5, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These 'PSE41-5' proteins include variants of SEQ ID NO: 5. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 5. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 5 while retaining at least one epitope of SEQ ID NO: 5. The final 40 C-terminal amino acids of SEQ ID NO: 5 can usefully be omitted. The first 37 N-terminal amino acids of SEQ ID NO: 5 can usefully be omitted. Other fragments omit one or more protein domains. 'PSE41-5' is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

20 [0057] SEQ ID NO: 40 is a useful fragment of SEQ ID NO: 5 ("PSE41-5"₃₈₋₃₁₇). This fragment includes the most exposed domain of 'PSE41-5' and is more easily used at an industrial scale. It also reduces the antigen's similarity with human proteins.

PA3526 or PSE44-4

25 [0058] The PSE44-4 antigen is annotated as 'probable outer membrane protein precursor'. In the PAO1 strain PSE44-4 is PA3526 and has amino acid sequence SEQ ID NO: 6 (GI: 15598722). See Ref 37.. Sometimes, PA3526 is referred to herein as 'PSE44-4 or 'PSE44'.

30 [0059] Useful PSE44-4 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 6 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 6; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 6, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE44-4 proteins include variants of SEQ ID NO: 6. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 6. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 6 while retaining at least one epitope of SEQ ID NO: 6. The first 19 N-terminal amino acids of SEQ ID NO: 6 can usefully be omitted. Other fragments omit one or more protein domains. PSE44-4 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

40 [0060] SEQ ID NO: 41 is a useful fragment of SEQ ID NO: 6 ('PSE44-4'₂₀₋₃₂₁). This fragment includes the most exposed domain of PSE44-4 and is more easily used at an industrial scale. It also reduces the antigen's similarity with human proteins.

PA4082 or PSE47A-2

45 [0061] The PSE47A-2 antigen is annotated as 'adhesive protein CupB5' or as "Serine protease". In the PAO1 strain PSE47A-2 is named PA4082 and has amino acid sequence SEQ ID NO: 7 (GI: 15599277). See Ref. 37. Sometimes, PA4082 is referred to herein as 'PSE47A' or 'PSE47A-2' (fragment).

50 [0062] Useful PSE47A-2 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 7 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 7; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 7, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE47A-2 proteins include variants of SEQ ID NO: 7. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 7. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 7 while retaining at least one epitope of SEQ ID NO: 7. Since the C- terminal portion of this protein is corresponding to the translocator domain, which is totally embedded in the outer membrane and therefore totally inaccessible to antibodies can be useful

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omitted. Hence, the final 435 C-terminal amino acids of SEQ ID NO: 7 can usefully be omitted. The first 53 N-terminal amino acids of SEQ ID NO: 7 can usefully be omitted. Other fragments omit one or more protein domains. PSE47A-2 is naturally a long protein and so the use of fragments is helpful *e.g.* for purification, handling, fusion, expression, *etc.*

[0063] SEQ ID NO: 42 is a useful fragment of SEQ ID NO: 7 ('PSE47A-2₅₄₋₅₈₃'). This fragment includes the most exposed domain of PSE47A-2 and is more easily used at an industrial scale. It also reduces the antigen's similarity with human proteins.

PA5047 or PSE53-1

[0064] The PSE53-1 antigen is annotated as 'hypothetical protein'. In the PAO1 strain PSE53-1 is PA5047 and has amino acid sequence SEQ ID NO: 9 (GI: 15600240). See Ref.37. Sometimes, PA5047 is referred to herein as 'PSE53-1 or 'PSE53'.

[0065] Useful PSE53-1 antigens can elicit an antibody (*e.g.* when administered to a human) that recognises SEQ ID NO: 9 and/or may comprise an amino acid sequence: (a) having 50% or more identity (*e.g.* 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 9; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 9, wherein 'n' is 7 or more (*e.g.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE53-1 proteins include variants of SEQ ID NO: 9. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 9. Other preferred fragments lack one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 9 while retaining at least one epitope of SEQ ID NO: 9. The final 40 C-terminal amino acids of SEQ ID NO: 9 can usefully be omitted. The first 18 N-terminal amino acids of SEQ ID NO: 9 can usefully be omitted. Other fragments omit one or more protein domains. PSE53-1 is naturally a long protein and so the use of fragments is helpful *e.g.* for purification, handling, fusion, expression, *etc.*

[0066] SEQ ID NO: 44 is a useful fragment of SEQ ID NO: 9 ('PSE53-1₁₉₋₄₇₉'). This fragment includes the most exposed domain of PSE53-1 and is more easily used at an industrial scale. It also reduces the antigen's similarity with human proteins.

PA5340 or PSE54

[0067] The PSE54 antigen is annotated as 'probable outer membrane protein precursor' and as 'hypothetical protein'. In the PAO1 strain PSE54 is PA3526 and has amino acid sequence SEQ ID NO: 10 (GI: 15598722). See Ref.37. Sometimes, PA5340 is referred to herein as 'PSE54'.

[0068] Useful PSE54 antigens can elicit an antibody (*e.g.* when administered to a human) that recognises SEQ ID NO: 10 and/or may comprise an amino acid sequence: (a) having 50% or more identity (*e.g.* 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 10; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 10, wherein 'n' is 7 or more (*e.g.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE54 proteins include variants of SEQ ID NO: 10. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 10. Other preferred fragments lack one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 10 while retaining at least one epitope of SEQ ID NO: 10. The final 40 C-terminal amino acids of SEQ ID NO: 10 can usefully be omitted. The first 16 N-terminal amino acids of SEQ ID NO: 10 can usefully be omitted. Other fragments omit one or more protein domains. PSE54 is naturally a long protein and so the use of fragments is helpful *e.g.* for purification, handling, fusion, expression, *etc.*

[0069] SEQ ID NO: 45 is a useful fragment of SEQ ID NO: 10 ('PSE54₁₇₋₂₄₃'). This fragment includes the most exposed domain of PSE54 and is more easily used at an industrial scale. It also reduces the antigen's similarity with human proteins.

PA0595 or PSE5-1

[0070] The PSE5-1 antigen is annotated as 'organic solvent tolerance protein OstA precursor'. In the PAO1 strain PSE5-1 is PA0595 and has amino acid sequence SEQ ID NO: 11 (GI: 15595792). See Ref.37. Sometimes, PA0595 is referred to herein as 'PSE5-1 or 'PSE5'.

[0071] Useful PSE5-1 antigens can elicit an antibody (*e.g.* when administered to a human) that recognises SEQ ID NO: 11 and/or may comprise an amino acid sequence: (a) having 50% or more identity (*e.g.* 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 11; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 11, wherein 'n' is 7 or more (*e.g.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE5-1 proteins include variants

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of SEQ ID NO: 11. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 11. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 11 while retaining at least one epitope of SEQ ID NO: 11. The final 40 C-terminal amino acids of SEQ ID NO: 11 can usefully be omitted. The first 33 N-terminal amino acids of SEQ ID NO: 11 can usefully be omitted. Other fragments omit one or more protein domains. PSE5-1 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0072] SEQ ID NO: 46 is a useful fragment of SEQ ID NO: 11 ('PSE5-1₃₄₋₉₂₄'). This fragment includes the most exposed domain of PSE5-1 and is more easily used at an industrial scale.

PA1954 or PSE13-2

[0073] The PSE13-2 antigen is annotated as 'hypothetical protein'. In the PAO1 strain PSE13-2 is PA1954 and has amino acid sequence SEQ ID NO: 12 (GI: 15597150). See Ref.37. Sometimes, PA1954 is referred to herein as 'PSE13-2' or 'PSE13'.

[0074] Useful PSE13-2 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 12 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 12; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 12, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE13-2 proteins include variants of SEQ ID NO: 12. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 12. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 12 while retaining at least one epitope of SEQ ID NO: 12. The final 40 C-terminal amino acids of SEQ ID NO: 12 can usefully be omitted. The first 24 N-terminal amino acids of SEQ ID NO: 12 can usefully be omitted. Other fragments omit one or more protein domains. PSE13-2 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0075] SEQ ID NO: 47 is a useful fragment of SEQ ID NO: 12 ('PSE13-2₂₅₋₃₄₀'). This fragment includes the most exposed domain of PSE13-2 and is more easily used at an industrial scale.

PA3692 or PSE17-1

[0076] The PSE17-1 antigen is annotated as 'Lipotoxin F, LptF'. In the PAO1 strain PSE17-1 is PA3692 and has amino acid sequence SEQ ID NO: 13 (GI: 15598888). See Ref.37. It has been described as belonging to Outer membrane protein and related peptidoglycan-associated (lipo) proteins as shown in reference 39. Sometimes, PA3692 is referred to herein as 'PSE17-1' or 'PSE17'.

[0077] Useful PSE17-1 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 13 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 13; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 13, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE17-1 proteins include variants of SEQ ID NO: 13. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 13. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 13 while retaining at least one epitope of SEQ ID NO: 13. The final 40 C-terminal amino acids of SEQ ID NO: 13 can usefully be omitted. The first 19 N-terminal amino acids of SEQ ID NO: 13 can usefully be omitted. Other fragments omit one or more protein domains. PSE17-1 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0078] SEQ ID NO: 48 is a useful fragment of SEQ ID NO: 13 ('PSE17-1₂₀₋₂₆₁'). This fragment includes the most exposed domain of PSE17-1 and is more easily used at an industrial scale.

PA4370 or PSE18-2

[0079] The PSE18-2 antigen is annotated as 'Insulin-cleaving metalloproteinase outer membrane protein precursor'. In the PAO1 strain PSE18-2 is PA4370 and has amino acid sequence SEQ ID NO: 14 (GI: 15599566). See Ref.37. It has been described as belonging to Outer membrane protein and in particular as insulin-cleaving metalloproteinase outer membrane protein (IcmP) as shown in reference 40. Sometimes, PA4370 is referred to herein as 'PSE18-2' or 'PSE18'.

[0080] Useful PSE18-2 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 14 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 14; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 14, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE18-2 proteins include variants of SEQ ID NO: 14. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 14. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 14 while retaining at least one epitope of SEQ ID NO: 14. The final 40 C-terminal amino acids of SEQ ID NO: 14 can usefully be omitted. The first 20 N-terminal amino acids of SEQ ID NO: 14 can usefully be omitted. Other fragments omit one or more protein domains. PSE18-2 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0081] SEQ ID NO: 49 is a useful fragment of SEQ ID NO: 14 ('PSE18-2₂₁₋₄₄₆'). This fragment includes the most exposed domain of PSE18-2 and is more easily used at an industrial scale.

PA4735 or PSE20-1

[0082] The PSE20-1 antigen is annotated as 'hypothetical protein'. In the PAO1 strain PSE20-1 is PA4735 and has amino acid sequence SEQ ID NO: 16 (GI: 15599929). See Ref. 37. Sometimes, PA4735 is referred to herein as 'PSE20-1' or 'PSE20'.

[0083] Useful PSE20-1 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 16 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 16; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 16, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE20-1 proteins include variants of SEQ ID NO: 16. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 16. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 16 while retaining at least one epitope of SEQ ID NO: 16. The final 40 C-terminal amino acids of SEQ ID NO: 16 can usefully be omitted. The first 19 N-terminal amino acids of SEQ ID NO: 16 can usefully be omitted. Other fragments omit one or more protein domains. PSE20-1 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0084] SEQ ID NO: 51 is a useful fragment of SEQ ID NO: 16 ('PSE20-1₂₀₋₁₀₈₈'). This fragment includes the most exposed domain of PSE20-1 and is more easily used at an industrial scale.

PA3647 or PSE23-1

[0085] The PSE23-1 antigen is annotated as 'hypothetical protein'. In the PAO1 strain PSE23-1 is PA3647 and has amino acid sequence SEQ ID NO: 17 (GI: 15598843). See Ref. 37. It has been described as probable outer membrane protein precursor or as OmpH gene and it was described as contaminant during the purification process of OprL as shown in reference 41. Sometimes, PA3647 is referred to herein as 'PSE23-1' or 'PSE23'.

[0086] Useful PSE20-1 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 17 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 17; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 17, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE20-1 proteins include variants of SEQ ID NO: 17. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 17. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 17 while retaining at least one epitope of SEQ ID NO: 17. The final 40 C-terminal amino acids of SEQ ID NO: 17 can usefully be omitted. The first 22 N-terminal amino acids of SEQ ID NO: 17 can usefully be omitted. Other fragments omit one or more protein domains. PSE23-1 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0087] SEQ ID NO: 52 is a useful fragment of SEQ ID NO: 17 ('PSE20-1₂₃₋₁₆₈'). This fragment includes the most exposed domain of PSE23-1 and is more easily used at an industrial scale.

PA0126 or PSE24-1

[0088] The PSE24-1 antigen is annotated as 'hypothetical protein'. In the PAO1 strain PSE24-1 is PA0126 and has amino acid sequence SEQ ID NO: 18 (GI: 15595324). See Ref. 37. Sometimes, PA0126 is referred to herein as 'PSE24-1' or 'PSE24'.

[0089] Useful PSE24-1 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 18 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 18; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 18, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE24-1 proteins include variants of SEQ ID NO: 18. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 18. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 18 while retaining at least one epitope of SEQ ID NO: 18. The first 19 N-terminal amino acids of SEQ ID NO: 18 can usefully be omitted. Other fragments omit one or more protein domains. PSE24-1 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0090] SEQ ID NO: 53 is a useful fragment of SEQ ID NO: 18 ('PSE24-1₂₀₋₂₀₆'). This fragment includes the most exposed domain of PSE24-1 and is more easily used at an industrial scale.

PA0189 or PSE25-1

[0091] The PSE25-1 antigen is annotated as 'probable porin'. In the PAO1 strain PSE25-1 is PA0189 and has amino acid sequence SEQ ID NO: 19 (GI: 15595387). See Ref. 37. Sometimes, PA0189 is referred to herein as 'PSE25-1' or 'PSE25'.

[0092] Useful PSE25-1 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 19 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 19; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 19, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE25-1 proteins include variants of SEQ ID NO: 19. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 19. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 19 while retaining at least one epitope of SEQ ID NO: 19. The first 25 N-terminal amino acids of SEQ ID NO: 19 can usefully be omitted. Other fragments omit one or more protein domains. PSE25-1 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0093] SEQ ID NO: 54 is a useful fragment of SEQ ID NO: 19 ('PSE25-1₂₆₋₄₅₂'). This fragment includes the most exposed domain of PSE25-1 and is more easily used at an industrial scale.

PA0274 or PSE26-1

[0094] The PSE26-1 antigen is annotated as 'hypothetical protein'. In the PAO1 strain PSE26-1 is PA0274 and has amino acid sequence SEQ ID NO: 20 (GI: 15595471). See Ref. 37. Sometimes, PA0274 is referred to herein as 'PSE26-1' or 'PSE26'.

[0095] Useful PSE26-1 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 20 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 20; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 20, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE26-1 proteins include variants of SEQ ID NO: 20. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 20. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 20 while retaining at least one epitope of SEQ ID NO: 20. The first 23 N-terminal amino acids of SEQ ID NO: 20 can usefully be omitted. Other fragments omit one or more protein domains. PSE26-1 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0096] SEQ ID NO: 55 is a useful fragment of SEQ ID NO: 20 ('PSE26-1₂₄₋₂₅₆'). This fragment includes the most exposed domain of PSE26-1 and is more easily used at an industrial scale.

PA0537 or PSE28-2

[0097] The PSE28-1 antigen is annotated as 'conserved hypothetical protein'. In the PAO1 strain PSE28-1 is PA0537 and has amino acid sequence SEQ ID NO: 21 (GI: 15595734). See Ref. 37. Sometimes, PA0537 is referred to herein as 'PSE28-1' or 'PSE28'.

[0098] Useful PSE28-1 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 21 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 21; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 21, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE28-1 proteins include variants of SEQ ID NO: 21. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 21. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 21 while retaining at least one epitope of SEQ ID NO: 21. The first 19 N-terminal amino acids of SEQ ID NO: 21 can usefully be omitted. Other fragments omit one or more protein domains. PSE28-1 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0099] SEQ ID NO: 56 is a useful fragment of SEQ ID NO: 21 ('PSE28-1₂₀₋₂₀₂'). This fragment includes the most exposed domain of PSE28-1 and is more easily used at an industrial scale.

PA0737 or PSE31-2

[0100] The PSE31-2 antigen is annotated as 'conserved hypothetical protein'. In the PAO1 strain PSE31-2 is PA0737 and has amino acid sequence SEQ ID NO: 22 (GI: 15595934). See Ref. 37. It has been described as up-regulated lipoproteins. See Ref. 42. Sometimes, PA0737 is referred to herein as 'PSE31-2' or 'PSE31'.

[0101] Useful PSE31-2 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 22 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 22; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 22, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE31-2 proteins include variants of SEQ ID NO: 22. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 22. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 22 while retaining at least one epitope of SEQ ID NO: 22. The first 19 N-terminal amino acids of SEQ ID NO: 22 can usefully be omitted. Other fragments omit one or more protein domains. PSE31-2 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0102] SEQ ID NO: 57 is a useful fragment of SEQ ID NO: 22 ('PSE31-2₂₀₋₁₅₁'). This fragment includes the most exposed domain of PSE31-2 and is more easily used at an industrial scale.

PA1086 or PSE33-2

[0103] The PSE33-2 antigen is annotated as 'flagellar hook-associated protein 1 FlgK'. In the PAO1 strain PSE33-2 is PA1086 and has amino acid sequence SEQ ID NO: 23 (GI: 15596283). See Ref. 37. Sometimes, PA1086 is referred to herein as 'PSE33-2' or 'PSE33'.

[0104] Useful PSE33-2 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 23 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 23; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 23, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE33-2 proteins include variants of SEQ ID NO: 23. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 23. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 23 while retaining at least one epitope of SEQ ID NO: 23. The first N-terminal amino acid of SEQ ID NO: 23 can usefully be omitted. Other fragments omit one or more protein domains. PSE33-2 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0105] SEQ ID NO: 58 is a useful fragment of SEQ ID NO: 23, wherein only the Met at position 1 of the polypeptide has been removed to allow proper cloning and expression in commonly known expression systems *i.e.* PET vector system. This fragment includes the most exposed domain of PSE31-2 and is more easily used at an industrial scale.

PA2793 or PSE42-1

[0106] The PSE42-1 antigen is annotated as 'hypothetical protein'. In the PAO1 strain PSE42-1 is PA2793 and has amino acid sequence SEQ ID NO: 27 (GI: 15597989). See Ref. 37. Sometimes, PA2793 is referred to herein as 'PSE42-1' or 'PSE42'.

[0107] PSORT available program has predicted this protein as lipoprotein and a Type II (lipoprotein) export signal predicted by LipoP by a cleavage after residue 20. See Ref. 37.

[0108] Useful PSE42-1 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 27 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 27; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 27, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE42-1 proteins include variants of SEQ ID NO: 27. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 27. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 27 while retaining at least one epitope of SEQ ID NO: 27. The first 20 N-terminal amino acids of SEQ ID NO: 27 can usefully be omitted. Other fragments omit one or more protein domains. PSE42-1 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0109] SEQ ID NO: 62 is a useful fragment of SEQ ID NO: 27 ('PSE42-1₂₁₋₃₄₄'). This fragment includes the most exposed domain of PSE42-1 and is more easily used at an industrial scale.

PA3535 or PSE45-2

[0110] The PSE45-2 antigen is annotated as 'probable outer membrane protein precursor'. In the PAO1 strain PSE45-2 is PA3535 and has amino acid sequence SEQ ID NO: 28 (GI: 15598731). See Ref. 37. Sometimes, PA3535 is referred to herein as 'PSE45-2' or 'PSE45'.

[0111] Useful PSE45-2 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 28 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 28; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 28, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE45-2 proteins include variants of SEQ ID NO: 28. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 28. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 28 while retaining at least one epitope of SEQ ID NO: 28. The first 30 N-terminal amino acids of SEQ ID NO: 28 can usefully be omitted. Other fragments omit one or more protein domains. PSE45-2 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0112] SEQ ID NO: 63 is a useful fragment of SEQ ID NO: 28 ('PSE45-2₃₁₋₉₉₅'). This fragment includes the most exposed domain of PSE45-2 and is more easily used at an industrial scale.

PA4578 or PSE50-1

[0113] The PSE50-1 antigen is annotated as 'hypothetical protein'. In the PAO1 strain PSE50-1 is PA4578 and has amino acid sequence SEQ ID NO: 29 (GI: 15599774). See Ref. 37. Sometimes, PA4578 is referred to herein as 'PSE50-1' or 'PSE50'.

[0114] Useful PSE50-1 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 29 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 29; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 29, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE50-1 proteins include variants of SEQ ID NO: 29. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 29. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 19, 20, 25 or more) from the N-terminus of SEQ ID NO: 29 while retaining at least one epitope of SEQ ID NO: 29. The first 19 N-terminal amino acids of SEQ ID NO: 29 can usefully be omitted. Other fragments omit one or more protein domains. PSE45-2 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0115] SEQ ID NO: 64 is a useful fragment of SEQ ID NO: 29 ('PSE50-1₂₀₋₁₆₂'). This fragment includes the most exposed domain of PSE50-1 and is more easily used at an industrial scale.

PA4667 or PSE51-4

[0116] The PSE51-4 antigen is annotated as 'hypothetical protein'. In the PAO1 strain PSE51-4 is PA4667 and has amino acid sequence SEQ ID NO: 30 (GI: 15599862). See Ref. 37. Sometimes, PA4667 is referred to herein as 'PSE51-4' or 'PSE51'.

[0117] Useful PSE51-4 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 30 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 30; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 30, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE51-4 proteins include variants of SEQ ID NO: 30. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 30. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 19, 20, 25, 30 or more) from the N-terminus of SEQ ID NO: 30 while retaining at least one epitope of SEQ ID NO: 30. The first 31 N-terminal amino acids of SEQ ID NO: 30 can usefully be omitted. Other fragments omit one or more protein domains. PSE51-4 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0118] SEQ ID NO: 65 is a useful fragment of SEQ ID NO: 30 ('PSE51-4₃₂₋₅₉₀'). This fragment includes the most exposed domain of PSE51-4 and is more easily used at an industrial scale.

PA1106 or PSE34-1

[0119] The PSE34-1 antigen is annotated as 'hypothetical protein'. In the PAO1 strain PSE34-1 is PA1106 and has amino acid sequence SEQ ID NO: 24 (GI: 15596303). See Ref. 37. Sometimes, PA1106 is referred to herein as 'PSE34-1' or 'PSE34'.

[0120] Useful PSE34-1 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 24 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 24; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 24, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE34-1 proteins include variants of SEQ ID NO: 24. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 24. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 24 while retaining at least one epitope of SEQ ID NO: 24. The first 20 N-terminal amino acids of SEQ ID NO: 24 can usefully be omitted. Other fragments omit one or more protein domains. PSE34-1 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0121] SEQ ID NO: 59 is a useful fragment of SEQ ID NO: 24 ('PSE34-1₂₁₋₂₃₇'). This fragment includes the most exposed domain of PSE34-1 and is more easily used at an industrial scale.

PA1324 or PSE36-3

[0122] The PSE36-3 antigen is annotated as 'hypothetical protein'. In the PAO1 strain PSE36-3 is PA1324 and has amino acid sequence SEQ ID NO: 25 (GI: 15596521). See Ref. 37. Sometimes, PA1324 is referred to herein as 'PSE36-3' or 'PSE36'.

[0123] PA1324 is postulated to be involved in the binding and transport of sugars or polysaccharides associated with the peptidoglycan matrix during biofilm formation. [43]

[0124] Useful PSE36-3 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 25 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 25; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 25, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE36-3 proteins include variants of SEQ ID NO: 25. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 25. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 25 while retaining at least one epitope of SEQ ID NO: 25. The first 19 N-terminal amino acids of SEQ ID NO: 25 can usefully be omitted. Other fragments omit one or more protein domains. PSE36-3 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0125] SEQ ID NO: 60 is a useful fragment of SEQ ID NO: 25 ('PSE36-3₂₀₋₁₇₀'). This fragment includes the most exposed domain of PSE36-3 and is more easily used at an industrial scale.

Second antigen group**PA1178 or PSE10**

5 **[0126]** The 'PSE10' antigen is annotated as 'PhoP/Q and low Mg²⁺ inducible outer membrane protein'. In the PAO1 strain PSE10 is called also as OprH [44] and has amino acid sequence SEQ ID NO: 2. In the PAO1 strain PSE10 is annotated as PA1178 and its NCBI identifier is GI: 15596375. See Ref. 37. Sometimes, PA1178 is referred to herein as 'PSE10-1' or 'PSE10'.

10 **[0127]** Useful PSE10 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 2 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 2; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 2, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE10 proteins include variants of SEQ ID NO: 2. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 2. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50 or more) from the N-terminus of SEQ ID NO: 2 while retaining at least one epitope of SEQ ID NO: 2. The first 21 N-terminal amino acids of SEQ ID NO: 2 can usefully be omitted. Other fragments omit one or more protein domains. The use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

20 **[0128]** SEQ ID NO: 37 is a useful fragment of SEQ ID NO: 2 ('PSE10₂₂₋₂₀₀'). This fragment includes the most exposed domain of PSE10 and is more easily used at an industrial scale.

PA1248 or PSE11-3

25 **[0129]** The 'PSE11-3' antigen is annotated as 'Alkaline protease secretion outer membrane protein AprF precursor'. In the PAO1 strain PSE11-3 is PA1248 and has amino acid sequence SEQ ID NO: 4. In the PAO1 strain the NCBI identifier is GI: 15596445. See reference 37 and 45.

[0130] Sometimes, PA1248 is referred to herein as 'PSE11-3' or 'PSE11'.

30 **[0131]** Useful PSE11-3 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 4 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 4; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 4, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE11-3 proteins include variants of SEQ ID NO: 4. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 4. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 4 while retaining at least one epitope of SEQ ID NO: 4. The first 18 N-terminal amino acids of SEQ ID NO: 4 can usefully be omitted. Other fragments omit one or more protein domains. PSE11-3 is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc. In reference 45 this antigen is described as a known virulence factor and tested as antigen.

40 **[0132]** SEQ ID NO: 39 is a useful fragment of SEQ ID NO: 4 ('PSE11-3₁₉₋₄₈₁'). This fragment includes the most exposed domain of PSE11-3 and is more easily used at an industrial scale.

PA4765 or PSE52-1

45 **[0133]** The PSE52-1 antigen is annotated as 'Outer membrane lipoprotein OmlA precursor'. In the PAO1 strain PSE52-1 is PA4765 and has amino acid sequence SEQ ID NO: 8 (GI: 15599959). See Ref. 37. Sometimes, PA4765 is referred to herein as 'PSE52-1' or 'PSE52'.

[0134] It has been described since 1999 as belonging to outer membrane protein family as in reference 46.

50 **[0135]** Useful PSE52-1 antigens can elicit an antibody (e.g. when administered to a human) that recognises SEQ ID NO: 8 and/or may comprise an amino acid sequence: (a) having 50% or more identity (e.g. 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 8; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 8, wherein 'n' is 7 or more (e.g. 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE52-1 proteins include variants of SEQ ID NO: 8. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 8. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 8 while retaining at least one epitope of SEQ ID NO: 8. The final 40 C-terminal amino acids of SEQ ID NO: 8 can usefully be omitted. The first 21 N-

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terminal amino acids of SEQ ID NO: 8 can usefully be omitted. Other fragments omit one or more protein domains. PSE52-1 is naturally a long protein and so the use of fragments is helpful *e.g.* for purification, handling, fusion, expression, *etc.*

[0136] SEQ ID NO: 43 is a useful fragment of SEQ ID NO: 8 ('PSE52-1₂₂₋₁₇₆'). This fragment includes the most exposed domain of PSE52-1 and is more easily used at an industrial scale.

PA4710 or PSE19-1

[0137] The PSE19-1 antigen is annotated as 'Heme/Hemoglobin uptake outer membrane receptor PhuR precursor'. In the PAO1 strain PSE19-1 is PA4710 and has amino acid sequence SEQ ID NO: 15 (GI: 15599904). See Ref. 37. Short peptides derived from said antigen have been proposed to show certain immunogenicity, however this antigen has not been tested as vaccine antigen in combination [47]. Sometimes, PA4710 is referred to herein as 'PSE19-1' or 'PSE19'.

[0138] Useful PSE19-1 antigens can elicit an antibody (*e.g.* when administered to a human) that recognises SEQ ID NO: 15 and/or may comprise an amino acid sequence: (a) having 50% or more identity (*e.g.* 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 15; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 15, wherein 'n' is 7 or more (*e.g.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE19-2 proteins include variants of SEQ ID NO: 15. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 15. Other preferred fragments lack one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 15 while retaining at least one epitope of SEQ ID NO: 15. The final 40 C-terminal amino acids of SEQ ID NO: 15 can usefully be omitted. The first 25 N-terminal amino acids of SEQ ID NO: 15 can usefully be omitted. Other fragments omit one or more protein domains. PSE19-1 is naturally a long protein and so the use of fragments is helpful *e.g.* for purification, handling, fusion, expression, *etc.*

[0139] SEQ ID NO: 50 is a useful fragment of SEQ ID NO: 15 ('PSE19-1₂₆₋₇₆₄'). This fragment includes the most exposed domain of PSE19-1 and is more easily used at an industrial scale.

PA1777 or PSE38-1

[0140] The PSE38-1 antigen is annotated as 'Major porin and structural outer membrane porin OprF precursor'. In the PAO1 strain PSE38-1 is PA1777 and has amino acid sequence SEQ ID NO: 26 (GI: 15596974). See Ref. 37 and 48. EP0297291 described for the first time this protein as useful antigen. Sometimes, PA1777 is referred to herein as 'PSE38-1' or 'PSE38'.

[0141] Useful PSE38-1 antigens can elicit an antibody (*e.g.* when administered to a human) that recognises SEQ ID NO: 26 and/or may comprise an amino acid sequence: (a) having 50% or more identity (*e.g.* 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 26; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 26, wherein 'n' is 7 or more (*e.g.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). These PSE38-1 proteins include variants of SEQ ID NO: 26. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 26. Other preferred fragments lack one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 26 while retaining at least one epitope of SEQ ID NO: 26. The first 24 N-terminal amino acids of SEQ ID NO: 26 can usefully be omitted. Other fragments omit one or more protein domains. PSE38-1 is naturally a long protein and so the use of fragments is helpful *e.g.* for purification, handling, fusion, expression, *etc.*

[0142] SEQ ID NO: 61 is a useful fragment of SEQ ID NO: 26 ('PSE38-1₂₅₋₃₅₀'). This fragment includes the most exposed domain of PSE38-1 and is more easily used at an industrial scale.

Further antigenic polypeptides

PA4525 or PilA

[0143] The PilA antigen is annotated as 'type 4 fimbrial precursor PilA'. In the PAO1 strain PilA is PA4525 and has amino acid sequence SEQ ID NO: 31 (GI: 15599721). See Ref. 37. Useful PilA antigens can elicit an antibody (*e.g.* when administered to a human) that recognises SEQ ID NO: 31 and/or may comprise an amino acid sequence: (a) having 50% or more identity (*e.g.* 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NO: 31; and/or (b) comprising a fragment of at least 'n' consecutive amino acids of SEQ ID NO: 31, wherein 'n' is 7 or more (*e.g.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200,

250 or more). These PilA proteins include variants of SEQ ID NO: 31. Preferred fragments of (b) comprise an epitope from SEQ ID NO: 31. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NO: 31 while retaining at least one epitope of SEQ ID NO: 31. Other fragments omit one or more protein domains. PilA is naturally a long protein and so the use of fragments is helpful e.g. for purification, handling, fusion, expression, etc.

[0144] Useful fragment include the most exposed domain of PilA and is more easily used at an industrial scale. It also reduces the antigen's similarity with human proteins. Vaccines and immunotherapy using this antigen have been attempted as shown in reference 49, and in reference 50.

OprF-OprI

[0145] The OmpF/I antigen is a fusion protein consisting of a hybrid protein [Met-Ala-(His)₆OprF (190-342)-OprI (21-83)], ("His)₆" disclosed as SEQ ID NO: 70), resulting by the fusion of the mature outer membrane protein I (OprI) and amino acids 190 to 342 of OprF of *Pseudomonas aeruginosa* expressed in *Escherichia coli* and purified.

[0146] The fusion protein has been described in reference 4 as SEQ ID NO 006. For reference purposes, a full-length amino acid sequence of the fusion protein described herein is given as SEQ ID NO: 32. This antigen can be usefully used as positive control as single antigen, or showing a surprising positive effect increasing vaccine efficacy in in vivo experiments when used in combination with specific pseudomonas antigens.

PA1092 or FliC (Flagellar protein)

[0147] Flagella and main flagella proteins like FliC (PA1092) or FliD (PA1094) have been extensively characterized and used as single vaccine antigens in the past as shown in reference 51. For reference purposes, a full-length amino acid sequence of FliC is given as SEQ ID NO: 33 herein.

[0148] PA1092 antigen and/or PA1094 antigen may be usefully combined with any of the "first antigen group" or the "second antigen group".

PA1094 or FliD (Flagellar protein)

[0149] Flagella and main flagella proteins like FliD (PA1094) have been extensively characterized and used as vaccine antigens in the past as shown in reference 51. For reference purposes, a full-length amino acid sequence of FliD is given as SEQ ID NO: 34 herein.

[0150] PA1094 may be usefully combined with any of the "first antigen group" or any of the "second antigen group".

PA1148 or Exoprotein A or Exotoxin A

[0151] The Exoprotein A known also as Exotoxin A is an exoprotein which has been extensively characterized and used primarily as carrier protein in polysaccharide conjugate vaccine approach, e.g. reference 22. It is known as PA1148 in the PAO1PAO1 strain. See Ref. 37.

[0152] PA1148 antigen may be usefully combined with any of the "first antigen group" or any of the "second antigen group".

Hybrid polypeptides

[0153] Antigens used in the invention may be present in the composition as individual separate polypeptides. Where more than one antigen is used, however, they do not have to be present as separate polypeptides. Instead, at least two (e.g. 2, 3, 4, 5, or more) antigens can be expressed as a single polypeptide chain (a 'hybrid' polypeptide). Hybrid polypeptides offer two main advantages: first, a polypeptide that may be unstable or poorly expressed on its own can be assisted by adding a suitable hybrid partner that overcomes the problem; second, commercial manufacture is simplified as only one expression and purification need be employed in order to produce two polypeptides which are both antigenically useful. The hybrid polypeptide may comprise two or more polypeptide sequences from the first antigen group. The hybrid polypeptide may comprise one or more polypeptide sequences from the first antigen group and one or more polypeptide sequences from the second antigen group. Moreover, the hybrid polypeptide may comprise two or more polypeptide sequences from each of the antigens listed above, or two or more variants of the same antigen in the cases in which the sequence has partial variability across strains.

[0154] Hybrids consisting of amino acid sequences from two, three, four, five, six, seven, eight, nine, or ten antigens are useful. In particular, hybrids consisting of amino acid sequences from two, three, four, or five antigens are preferred,

such as two or three antigens.

[0155] Different hybrid polypeptides may be mixed together in a single formulation. Hybrids may be combined with non-hybrid antigens selected from the first, second or third antigen groups. Within such combinations, an antigen may be present in more than one hybrid polypeptide and/or as a non-hybrid polypeptide. It is preferred, however, that an antigen is present either as a hybrid or as a non-hybrid, but not as both.

[0156] The hybrid polypeptides can also be combined with conjugates or non-*P.aeruginosa* antigens as described above.

[0157] Hybrid polypeptides can be represented by the formula $\text{NH}_2\text{-A}\{-\text{X-L}\}_n\text{-B-COOH}$, wherein: X is an amino acid sequence of a *P. aeruginosa* antigen, as described above; L is an optional linker amino acid sequence; A is an optional N-terminal amino acid sequence; B is an optional C-terminal amino acid sequence; *n* is an integer of 2 or more (e.g. 2, 3, 4, 5, 6, etc.). Usually *n* is 2 or 3.

[0158] If a -X- moiety has a leader peptide sequence in its wild-type form, this may be included or omitted in the hybrid protein. In some embodiments, the leader peptides will be deleted except for that of the -X- moiety located at the N-terminus of the hybrid protein *i.e.* the leader peptide of X_1 will be retained, but the leader peptides of $X_2 \dots X_n$ will be omitted. This is equivalent to deleting all leader peptides and using the leader peptide of X_1 as moiety -A-.

[0159] For each *n* instances of {-X-L-}, linker amino acid sequence -L- may be present or absent. For instance, when *n*=2 the hybrid may be $\text{NH}_2\text{-X}_1\text{-L}_1\text{-X}_2\text{-L}_2\text{-COOH}$, $\text{NH}_2\text{-X}_1\text{-X}_2\text{-COOH}$, $\text{NH}_2\text{-X}_1\text{-L}_1\text{-X}_2\text{-COOH}$, $\text{NH}_2\text{-X}_1\text{-X}_2\text{-L}_2\text{-COOH}$, etc. Linker amino acid sequence(s) -L- will typically be short (e.g. 20 or fewer amino acids *i.e.* 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1). Examples comprise short peptide sequences which facilitate cloning, poly-glycine linkers (*i.e.* comprising Gly_n where *n* = 2, 3, 4, 5, 6, 7, 8, 9, 10 or more) (SEQ ID NO: 71), and histidine tags (*i.e.* His_n where *n* = 3, 4, 5, 6, 7, 8, 9, 10 or more) (SEQ ID NO: 72). Other suitable linker amino acid sequences will be apparent to those skilled in the art. A useful linker is GSGGGG (SEQ ID NO: 67) or GSGSGGGG (SEQ ID NO: 68), with the Gly-Ser dipeptide being formed from a *Bam*HI restriction site, thus aiding cloning and manipulation, and the $(\text{Gly})_4$ (SEQ ID NO: 73) tetrapeptide being a typical poly-glycine linker. Other suitable linkers, particularly for use as the final L_n are ASGGGS (SEQ ID NO: 69) or a Leu-Glu dipeptide.

[0160] -A- is an optional N-terminal amino acid sequence. This will typically be short (e.g. 40 or fewer amino acids *i.e.* 40, 39, 38, 37, 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1). Examples include leader sequences to direct protein trafficking, or short peptide sequences which facilitate cloning or purification (e.g. histidine tags *i.e.* His_n where *n* = 3, 4, 5, 6, 7, 8, 9, 10 or more) (SEQ ID NO: 72). A useful tag contains a sequence of 6 consecutive Histidine (SEQ ID NO: 70), having at its start a homologue or heterologous start Methionine and/or an Alanine, *i.e.* SEQ ID NO 66. Other suitable N-terminal amino acid sequences will be apparent to those skilled in the art. If X_1 lacks its own N-terminus methionine, -A- is preferably an oligopeptide (e.g. with 1, 2, 3, 4, 5, 6, 7 or 8 amino acids) which provides a N-terminus methionine e.g. Met-Ala-Ser, or a single Met residue.

[0161] -B- is an optional C-terminal amino acid sequence. This will typically be short (e.g. 40 or fewer amino acids *i.e.* 39, 38, 37, 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1).

Polypeptides used with the invention

[0162] Polypeptides used with the invention can take various forms (e.g. native, fusions, glycosylated, non-glycosylated, lipidated, non-lipidated, phosphorylated, non-phosphorylated, myristoylated, non-myristoylated, monomeric, multimeric, particulate, denatured, etc.).

[0163] Polypeptides used with the invention can be prepared by various means (e.g. recombinant expression, purification from cell culture, chemical synthesis, isolated from a natural biological source etc.). Recombinantly-expressed proteins are preferred, particularly for hybrid polypeptides.

[0164] Polypeptides used with the invention are preferably provided in purified or substantially purified form *i.e.* substantially free from other polypeptides (e.g. free from naturally-occurring polypeptides), particularly from other pseudomonas or host cell polypeptides, and are generally at least about 50% pure (by weight), and usually at least about 90% pure *i.e.* less than about 50%, and more preferably less than about 10% (e.g. 5%) of a composition is made up of other expressed polypeptides. Thus the antigens in the compositions are separated from the whole organism with which the molecule is expressed.

[0165] Polypeptides used with the invention are preferably pseudomonas polypeptides.

[0166] The term "polypeptide" refers to amino acid polymers of any length. The polymer may be linear or branched, it may comprise modified amino acids, and it may be interrupted by non-amino acids. The terms also encompass an amino acid polymer that has been modified naturally or by intervention; for example, disulfide bond formation, glycosylation, lipidation, acetylation, phosphorylation, or any other manipulation or modification, such as conjugation with a labelling component. Also included are, for example, polypeptides containing one or more analogs of an amino acid (including, for example, unnatural amino acids, etc.), as well as other modifications known in the art. Polypeptides can

occur as single chains or associated chains.

[0167] The invention provides polypeptides comprising a sequence -P-Q- or -Q-P-, wherein: -P- is an amino acid sequence as defined above and -Q- is not a sequence as defined above *i.e.* the invention provides fusion proteins. Where the N-terminus codon of -P- is not ATG, but this codon is not present at the N-terminus of a polypeptide, it will be translated as the standard amino acid for that codon rather than as a Met. Where this codon is at the N-terminus of a polypeptide, however, it will be translated as Met. Examples of -Q- moieties include, but are not limited to, histidine tags (*i.e.* His_n where *n* = 3, 4, 5, 6, 7, 8, 9, 10 or more) (SEQ ID NO: 72), maltose-binding protein, or glutathione-S-transferase (GST).

[0168] The invention also provides a process for producing a polypeptide of the invention, comprising the step of culturing a host cell transformed with nucleic acid of the invention under conditions which induce polypeptide expression.

[0169] Although expression of the polypeptides of the invention may take place in a *Pseudomonas*, the invention will usually use a heterologous host for expression (recombinant expression). The heterologous host may be prokaryotic (*e.g.* a bacterium) or eukaryotic. It may be *E.coli*, but other suitable hosts include *Bacillus subtilis*, *Vibrio cholerae*, *Salmonella typhi*, *Salmonella typhimurium*, *Neisseria lactamica*, *Neisseria cinerea*, *Mycobacteria* (*e.g.* *M.tuberculosis*), yeasts, *etc.* Compared to the wild-type *P. aeruginosa* genes encoding polypeptides of the invention, it is helpful to change codons to optimise expression efficiency in such hosts without affecting the encoded amino acids.

[0170] The invention provides a process for producing a polypeptide of the invention, comprising the step of synthesising at least part of the polypeptide by chemical means.

20 **Nucleic acids**

[0171] The invention also provides nucleic acid encoding polypeptides and hybrid polypeptides of the invention. It also provides nucleic acid comprising a nucleotide sequence that encodes one or more polypeptides or hybrid polypeptides of the invention.

[0172] The invention also provides nucleic acid comprising nucleotide sequences having sequence identity to such nucleotide sequences. Identity between sequences is preferably determined by the Smith-Waterman homology search algorithm as described above. Such nucleic acids include those using alternative codons to encode the same amino acid.

[0173] The invention also provides nucleic acid which can hybridize to these nucleic acids. Hybridization reactions can be performed under conditions of different "stringency". Conditions that increase stringency of a hybridization reaction are widely known and published in the art. Examples of relevant conditions include (in order of increasing stringency): incubation temperatures of 25°C, 37°C, 50°C, 55°C and 68°C; buffer concentrations of 10 x SSC, 6 x SSC, 1 x SSC, 0.1 x SSC (where SSC is 0.15 M NaCl and 15 mM citrate buffer) and their equivalents using other buffer systems; formamide concentrations of 0%, 25%, 50%, and 75%; incubation times from 5 minutes to 24 hours; 1, 2, or more washing steps; wash incubation times of 1, 2, or 15 minutes; and wash solutions of 6 x SSC, 1 x SSC, 0.1 x SSC, or de-ionized water. Hybridization techniques and their optimization are well known in the art.

[0174] In some embodiments, nucleic acid of the invention hybridizes to a target under low stringency conditions; in other embodiments it hybridizes under intermediate stringency conditions; in preferred embodiments, it hybridizes under high stringency conditions. An exemplary set of low stringency hybridization conditions is 50°C and 10 x SSC. An exemplary set of intermediate stringency hybridization conditions is 55°C and 1 x SSC. An exemplary set of high stringency hybridization conditions is 68°C and 0.1 x SSC.

[0175] The invention includes nucleic acid comprising sequences complementary to these sequences (*e.g.* for antisense or probing, or for use as primers).

[0176] Nucleic acids of the invention can be used in hybridisation reactions (*e.g.* Northern or Southern blots, or in nucleic acid microarrays or 'gene chips') and amplification reactions (*e.g.* PCR, SDA, SSSR, LCR, TMA, NASBA, *etc.*) and other nucleic acid techniques.

[0177] Nucleic acid according to the invention can take various forms (*e.g.* single-stranded, double-stranded, vectors, primers, probes, labelled *etc.*). Nucleic acids of the invention may be circular or branched, but will generally be linear. Unless otherwise specified or required, any embodiment of the invention that utilizes a nucleic acid may utilize both the double-stranded form and each of two complementary single-stranded forms which make up the double-stranded form. Primers and probes are generally single-stranded, as are antisense nucleic acids.

[0178] Nucleic acids of the invention are preferably provided in purified or substantially purified form *i.e.* substantially free from other nucleic acids (*e.g.* free from naturally-occurring nucleic acids), particularly from other *pseudomonas* or host cell nucleic acids, generally being at least about 50% pure (by weight), and usually at least about 90% pure. Nucleic acids of the invention are preferably *pseudomonas* nucleic acids.

[0179] Nucleic acids of the invention may be prepared in many ways *e.g.* by chemical synthesis (*e.g.* phosphoramidite synthesis of DNA) in whole or in part, by digesting longer nucleic acids using nucleases (*e.g.* restriction enzymes), by joining shorter nucleic acids or nucleotides (*e.g.* using ligases or polymerases), from genomic or cDNA libraries, *etc.*

[0180] Nucleic acid of the invention may be attached to a solid support (*e.g.* a bead, plate, filter, film, slide, microarray

support, resin, etc.). Nucleic acid of the invention may be labelled e.g. with a radioactive or fluorescent label, or a biotin label. This is particularly useful where the nucleic acid is to be used in detection techniques e.g. where the nucleic acid is a primer or as a probe.

[0181] The term "nucleic acid" includes in general means a polymeric form of nucleotides of any length, which contain deoxyribonucleotides, ribonucleotides, and/or their analogs. It includes DNA, RNA, DNA/RNA hybrids. It also includes DNA or RNA analogs, such as those containing modified backbones (e.g. peptide nucleic acids (PNAs) or phosphorothioates) or modified bases. Thus the invention includes mRNA, tRNA, rRNA, ribozymes, DNA, cDNA, recombinant nucleic acids, branched nucleic acids, plasmids, vectors, probes, primers, etc. Where nucleic acid of the invention takes the form of RNA, it may or may not have a 5' cap.

[0182] Nucleic acids of the invention may be part of a vector i.e. part of a nucleic acid construct designed for transduction/transfection of one or more cell types. Vectors may be, for example, "cloning vectors" which are designed for isolation, propagation and replication of inserted nucleotides, "expression vectors" which are designed for expression of a nucleotide sequence in a host cell, "viral vectors" which is designed to result in the production of a recombinant virus or virus-like particle, or "shuttle vectors", which comprise the attributes of more than one type of vector. Preferred vectors are plasmids. A "host cell" includes an individual cell or cell culture which can be or has been a recipient of exogenous nucleic acid. Host cells include progeny of a single host cell, and the progeny may not necessarily be completely identical (in morphology or in total DNA complement) to the original parent cell due to natural, accidental, or deliberate mutation and/or change. Host cells include cells transfected or infected *in vivo* or *in vitro* with nucleic acid of the invention.

[0183] Where a nucleic acid is DNA, it will be appreciated that "U" in a RNA sequence will be replaced by "T" in the DNA. Similarly, where a nucleic acid is RNA, it will be appreciated that "T" in a DNA sequence will be replaced by "U" in the RNA.

[0184] The term "complement" or "complementary" when used in relation to nucleic acids refers to Watson-Crick base pairing. Thus the complement of C is G, the complement of G is C, the complement of A is T (or U), and the complement of T (or U) is A. It is also possible to use bases such as I (the purine inosine) e.g. to complement pyrimidines (C or T).

[0185] Nucleic acids of the invention can be used, for example: to produce polypeptides; as hybridization probes for the detection of nucleic acid in biological samples; to generate additional copies of the nucleic acids; to generate ribozymes or antisense oligonucleotides; as single-stranded DNA primers or probes; or as triple-strand forming oligonucleotides.

[0186] The invention provides a process for producing nucleic acid of the invention, wherein the nucleic acid is synthesised in part or in whole using chemical means.

[0187] The invention provides vectors comprising nucleotide sequences of the invention (e.g. cloning or expression vectors) and host cells transformed with such vectors.

[0188] Nucleic acid amplification according to the invention may be quantitative and/or real-time.

[0189] For certain embodiments of the invention, nucleic acids are preferably at least 7 nucleotides in length (e.g. 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 45, 50, 55, 60, 65, 70, 75, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 225, 250, 275, 300 nucleotides or longer).

[0190] For certain embodiments of the invention, nucleic acids are preferably at most 500 nucleotides in length (e.g. 450, 400, 350, 300, 250, 200, 150, 140, 130, 120, 110, 100, 90, 80, 75, 70, 65, 60, 55, 50, 45, 40, 39, 38, 37, 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15 nucleotides or shorter).

[0191] Primers and probes of the invention, and other nucleic acids used for hybridization, are preferably between 10 and 30 nucleotides in length (e.g. 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 40 or more nucleotides).

Strains and variants

[0192] Antigens are defined above by reference to existing nomenclature (e.g. "PA0328"), to "PSE52" or to "PSE followed by a natural number, indicating the clone number, i.e. PSE52-1, etc" or to the respective SEQ ID NOs numbers.

[0193] Table 1 below associates these three naming/numbering systems to existing PAO1 public available numbering.

[0194] PAO1 numbering refers to the genome of *P. aeruginosa* strain PAO1 which is extensively described in terms of genomic analysis in reference 37.

[0195] Functional annotations for each antigen are also given in the databases.

[0196] Thus an exemplary amino acid and nucleotide sequence for any of these antigens can easily be found in public sequence databases from the PAO1 strain, but the invention is not limited to sequences from the PAO1 strains. Standard search and alignment techniques can be used to identify in any of these (or other) further genome sequences the homolog of any particular sequence from the PAO1 strain. Moreover, the available sequences from the PAO1 strain can be used to design primers for amplification of homologous sequences from other strains. Thus the invention is not limited to this strain, but rather encompasses such variants and homologs from other strains of *P. aeruginosa*, as well as non-natural

variants. In general, suitable variants of a particular SEQ ID NO include its allelic variants, its polymorphic forms, its homologs, its orthologs, its paralogs, its mutants, etc.

[0197] Thus, for instance, polypeptides used with the invention may, compared to the SEQ ID NO herein, include one or more (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, etc.) amino acid substitutions, such as conservative substitutions (i.e. substitutions of one amino acid with another which has a related side chain). Genetically-encoded amino acids are generally divided into four families: (1) acidic i.e. aspartate, glutamate; (2) basic i.e. lysine, arginine, histidine; (3) non-polar i.e. alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan; and (4) uncharged polar i.e. glycine, asparagine, glutamine, cysteine, serine, threonine, tyrosine. Phenylalanine, tryptophan, and tyrosine are sometimes classified jointly as aromatic amino acids. In general, substitution of single amino acids within these families does not have a major effect on the biological activity. The polypeptides may also include one or more (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, etc.) single amino acid deletions relative to the SEQ ID NO sequences. The polypeptides may also include one or more (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, etc.) insertions (e.g. each of 1, 2, 3, 4 or 5 amino acids) relative to the SEQ ID NO sequences.

[0198] Similarly, a polypeptide used with the invention may comprise an amino acid sequence that:

- is identical (i.e. 100% identical) to a sequence disclosed in the sequence listing;
- shares sequence identity (e.g. 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) with a sequence disclosed in the sequence listing;
- has 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 (or more) single amino acid alterations (deletions, insertions, substitutions), which may be at separate locations or may be contiguous, as compared to the sequences of (a) or (b);
- when aligned with a particular sequence from the sequence listing using a pairwise alignment algorithm, each moving window of x amino acids from N-terminus to C-terminus (such that for an alignment that extends to p amino acids, where $p > x$, there are $p-x+1$ such windows) has at least $x \cdot y$ identical aligned amino acids, where: x is selected from 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200; y is selected from 0.50, 0.60, 0.70, 0.75, 0.80, 0.85, 0.90, 0.91, 0.92, 0.93, 0.94, 0.95, 0.96, 0.97, 0.98, 0.99; and if $x \cdot y$ is not an integer then it is rounded up to the nearest integer. The preferred pairwise alignment algorithm is the Needleman-Wunsch global alignment algorithm [52], using default parameters (e.g. with Gap opening penalty = 10.0, and with Gap extension penalty = 0.5, using the EBLOSUM62 scoring matrix). This algorithm is conveniently implemented in the *needle* tool in the EMBOSS package [53].

[0199] Where hybrid polypeptides are used, the individual antigens within the hybrid (i.e. individual -X-moieties) may be from one or more strains. Where $n=2$, for instance, X_2 may be from the same strain as X_1 or from a different strain. Where $n=3$, the strains might be (i) $X_1=X_2=X_3$ (ii) $X_1=X_2 \neq X_3$ (iii) $X_1 \neq X_2 = X_3$ (iv) $X_1 \neq X_2 \neq X_3$ or (v) $X_1 = X_3 \neq X_2$, etc.

[0200] Within group (c), deletions or substitutions may be at the N-terminus and/or C-terminus, or may be between the two termini. Thus a truncation is an example of a deletion. Truncations may involve deletion of up to 40 (or more) amino acids at the N-terminus and/or C-terminus. N-terminus truncation can remove leader peptides e.g. to facilitate recombinant expression in a heterologous host. C-terminus truncation can remove anchor sequences e.g. to facilitate recombinant expression in a heterologous host.

[0201] In general, when an antigen comprises a sequence that is not identical to a complete *P. aeruginosa* sequence from the sequence listing (e.g. when it comprises a sequence listing with <100% sequence identity thereto, or when it comprises a fragment thereof) it is preferred in each individual instance that the antigen can elicit an antibody which recognises the respective complete *P. aeruginosa* sequence.

Mutant bacteria

[0202] Present invention, also provides a *P. aeruginosa* bacterium in which one or more of the antigens from the various antigen groups of the invention has/have been knocked out (see Ref. 46). Techniques for producing knockout bacteria are well known, and knockout of genes from *P. aeruginosa* strains have been reported i.e. in Ref. 54. A knockout mutation may be situated in the coding region of the gene or may lie within its transcriptional control regions (e.g. within its promoter). A knockout mutation will reduce the level of mRNA encoding the antigen to <1% of that produced by the wild-type bacterium, preferably <0.5%, more preferably <0.1%, and most preferably to 0%.

[0203] The invention also provides a *P. aeruginosa* in which one or more of the antigens from the various antigen groups of the invention has a mutation which inhibits its activity. The gene encoding the antigen will have a mutation that changes the encoded amino acid sequence. Mutation may involve deletion, substitution, and/or insertion, any of which may be involve one or more amino acids.

[0204] The invention also provides a bacterium, such as a *P. aeruginosa* bacterium, which hyper-expresses an antigen of the invention.

[0205] The invention also provides a bacterium, such as a *P. aeruginosa* bacterium, that constitutively expresses an antigen of the invention. The invention also provides a *E. coli* comprising a gene encoding an antigen of the invention,

wherein the gene is under the control of an inducible promoter.

[0206] Mutant bacteria are particularly useful for preparing bacterial outer membrane vesicles which include *P. aeruginosa* antigens (e.g. antigens of the invention), which can be used as immunogens [55-57].

5 **Immunogenic compositions and medicaments**

[0207] Immunogenic compositions of the invention may be useful as vaccines. Vaccines according to the invention may either be prophylactic (*i.e.* to prevent infection) or therapeutic (*i.e.* to treat infection), but will typically be prophylactic.

[0208] Compositions may thus be pharmaceutically acceptable. They will usually include components in addition to the antigens e.g. they typically include one or more pharmaceutical carrier(s) and/or excipient(s).

[0209] Compositions will generally be administered to a mammal in aqueous form Prior to administration, however, the composition may have been in a non-aqueous form For instance, although some vaccines are manufactured in aqueous form, then filled and distributed and administered also in aqueous form, other vaccines are lyophilised during manufacture and are reconstituted into an aqueous form at the time of use. Thus a composition of the invention may be dried, such as a lyophilised formulation.

[0210] The composition may include preservatives such as thiomersal or 2-phenoxyethanol. It is preferred, however, that the vaccine should be substantially free from (*i.e.* less than 5µg/ml) mercurial material e.g. thiomersal-free. Vaccines containing no mercury are more preferred. Preservative-free vaccines are particularly preferred.

[0211] To improve thermal stability, a composition may include a temperature protective agent. Further details of such agents are provided below.

[0212] To control tonicity, it is preferred to include a physiological salt, such as a sodium salt. Sodium chloride (NaCl) is preferred, which may be present at between 1 and 20 mg/ml e.g. about 10±2mg/ml NaCl. Other salts that may be present include potassium chloride, potassium dihydrogen phosphate, disodium phosphate dehydrate, magnesium chloride, calcium chloride, *etc.*

[0213] Compositions will generally have an osmolality of between 200 mOsm/kg and 400 mOsm/kg, preferably between 240-360 mOsm/kg, and will more preferably fall within the range of 290-310 mOsm/kg.

[0214] Compositions may include one or more buffers. Typical buffers include: a phosphate buffer; a Tris buffer; a borate buffer; a succinate buffer; a histidine buffer (particularly with an aluminum hydroxide adjuvant); or a citrate buffer. Buffers will typically be included in the 5-20mM range.

[0215] The pH of a composition will generally be between 5.0 and 8.1, and more typically between 6.0 and 8.0 e.g. 6.5 and 7.5, or between 7.0 and 7.8.

[0216] The composition is preferably sterile. The composition is preferably non-pyrogenic e.g. containing <1 EU (endotoxin unit, a standard measure) per dose, and preferably <0.1 EU per dose. The composition is preferably gluten free.

[0217] The composition may include material for a single immunisation, or may include material for multiple immunisations (*i.e.* a 'multidose' kit). The inclusion of a preservative is preferred in multidose arrangements. As an alternative (or in addition) to including a preservative in multidose compositions, the compositions may be contained in a container having an aseptic adaptor for removal of material.

[0218] Human vaccines are typically administered in a dosage volume of about 0.5ml, although a half dose (*i.e.* about 0.25ml) may be administered to children.

[0219] Immunogenic compositions of the invention may also comprise one or more immunoregulatory agents. Preferably, one or more of the immunoregulatory agents include one or more adjuvants. The adjuvants may include a TH1 adjuvant and/or a TH2 adjuvant, or a TLR7 agonist further discussed below.

[0220] Thus the invention provides an immunogenic composition comprising a combination of:

- (1) one or more antigen(s) selected from the first, second, and further antigen group (as defined above); and
- (2) an adjuvant, such as an aluminium hydroxide adjuvant (for example, one or more antigens may be adsorbed to aluminium hydroxide).

[0221] For instance, the invention provides an immunogenic composition comprising a combination of a sta006 antigen and an adjuvant, such as an aluminium hydroxide adjuvant Similarly, the invention provides an immunogenic composition comprising a combination of a sta011 antigen and an adjuvant, such as an aluminium hydroxide adjuvant. These compositions are ideally buffered e.g. with a histidine buffer.

[0222] Adjuvants which may be used in compositions of the invention include, but are not limited to:

55 **A. Mineral-containing compositions**

[0223] Mineral containing compositions suitable for use as adjuvants in the invention include mineral salts, such as aluminium salts and calcium salts (or mixtures thereof). Calcium salts include calcium phosphate (e.g. the "CAP" particles

disclosed in ref. 58). Aluminum salts include hydroxides, phosphates, sulfates, *etc.*, with the salts taking any suitable form (*e.g.* gel, crystalline, amorphous, *etc.*). Adsorption to these salts is preferred (*e.g.* all antigens may be adsorbed). The mineral containing compositions may also be formulated as a particle of metal salt [59].

[0224] The adjuvants known as aluminum hydroxide and aluminum phosphate may be used. The invention can use any of the "hydroxide" or "phosphate" adjuvants that are in general use as adjuvants. The adjuvants known as "aluminium hydroxide" are typically aluminium oxyhydroxide salts, which are usually at least partially crystalline. The adjuvants known as "aluminium phosphate" are typically aluminium hydroxyphosphates, often also containing a small amount of sulfate (*i.e.* aluminium hydroxyphosphate sulfate). They may be obtained by precipitation, and the reaction conditions and concentrations during precipitation influence the degree of substitution of phosphate for hydroxyl in the salt.

[0225] A fibrous morphology (*e.g.* as seen in transmission electron micrographs) is typical for aluminium hydroxide adjuvants. The pl of aluminium hydroxide adjuvants is typically about 11 *i.e.* the adjuvant itself has a positive surface charge at physiological pH. Adsorptive capacities of between 1.8-2.6 mg protein per mg Al⁺⁺⁺ at pH 7.4 have been reported for aluminium hydroxide adjuvants.

[0226] Aluminium phosphate adjuvants generally have a PO₄/Al molar ratio between 0.3 and 1.2, preferably between 0.8 and 1.2, and more preferably 0.95±0.1. The aluminium phosphate will generally be amorphous, particularly for hydroxyphosphate salts. A typical adjuvant is amorphous aluminium hydroxyphosphate with PO₄/Al molar ratio between 0.84 and 0.92, included at 0.6mg Al³⁺/ml. The aluminium phosphate will generally be particulate (*e.g.* plate-like morphology as seen in transmission electron micrographs). Typical diameters of the particles are in the range 0.5-20µm (*e.g.* about 5-10µm) after any antigen adsorption. Adsorptive capacities of between 0.7-1.5 mg protein per mg Al⁺⁺⁺ at pH 7.4 have been reported for aluminium phosphate adjuvants.

[0227] The point of zero charge (PZC) of aluminium phosphate is inversely related to the degree of substitution of phosphate for hydroxyl, and this degree of substitution can vary depending on reaction conditions and concentration of reactants used for preparing the salt by precipitation. PZC is also altered by changing the concentration of free phosphate ions in solution (more phosphate = more acidic PZC) or by adding a buffer such as a histidine buffer (makes PZC more basic). Aluminium phosphates used according to the invention will generally have a PZC of between 4.0 and 7.0, more preferably between 5.0 and 6.5 *e.g.* about 5.7.

[0228] Suspensions of aluminium salts used to prepare compositions of the invention may contain a buffer (*e.g.* a phosphate or a histidine or a Tris buffer), but this is not always necessary. The suspensions are preferably sterile and pyrogen-free. A suspension may include free aqueous phosphate ions *e.g.* present at a concentration between 1.0 and 20 mM, preferably between 5 and 15 mM, and more preferably about 10 mM. The suspensions may also comprise sodium chloride.

[0229] The invention can use a mixture of both an aluminium hydroxide and an aluminium phosphate. In this case there may be more aluminium phosphate than hydroxide *e.g.* a weight ratio of at least 2:1 *e.g.* ≥5:1, ≥6:1, ≥7:1, ≥8:1, ≥9:1, *etc.*

[0230] The concentration of Al⁺⁺⁺ in a composition for administration to a patient is preferably less than 10mg/ml *e.g.* ≤5 mg/ml, ≤4 mg/ml, ≤3 mg/ml, ≤2 mg/ml, ≤1 mg/ml, *etc.* A preferred range is between 0.3 and 1mg/ml. A maximum of 0.85mg/dose is preferred.

B. Oil Emulsions

[0231] Oil emulsion compositions suitable for use as adjuvants in the invention include squalene-water emulsions, such as MF59 [Chapter 10 of ref. 63; see also ref. 60] (5% Squalene, 0.5% Tween 80, and 0.5% Span 85, formulated into submicron particles using a microfluidizer). Complete Freund's adjuvant (CFA) and incomplete Freund's adjuvant (IFA) may also be used.

[0232] Various oil-in-water emulsion adjuvants are known, and they typically include at least one oil and at least one surfactant, with the oil(s) and surfactant(s) being biodegradable (metabolizable) and biocompatible.

[0233] The oil droplets in the emulsion are generally less than 5µm in diameter, and ideally have a sub-micron diameter, with these small sizes being achieved with a microfluidiser to provide stable emulsions. Droplets with a size less than 220nm are preferred as they can be subjected to filter sterilization.

[0234] The emulsion can comprise oils such as those from an animal (such as fish) or vegetable source. Sources for vegetable oils include nuts, seeds and grains. Peanut oil, soybean oil, coconut oil, and olive oil, the most commonly available, exemplify the nut oils. Jojoba oil can be used *e.g.* obtained from the jojoba bean. Seed oils include safflower oil, cottonseed oil, sunflower seed oil, sesame seed oil and the like. In the grain group, corn oil is the most readily available, but the oil of other cereal grains such as wheat, oats, rye, rice, teff, triticale and the like may also be used. 6-10 carbon fatty acid esters of glycerol and 1,2-propanediol, while not occurring naturally in seed oils, may be prepared by hydrolysis, separation and esterification of the appropriate materials starting from the nut and seed oils. Fats and oils from mammalian milk are metabolizable and may therefore be used in the practice of this invention. The procedures for separation, purification, saponification and other means necessary for obtaining pure oils from animal sources are well

known in the art. Most fish contain metabolizable oils which may be readily recovered. For example, cod liver oil, shark liver oils, and whale oil such as spermaceti exemplify several of the fish oils which may be used herein. A number of branched chain oils are synthesized biochemically in 5-carbon isoprene units and are generally referred to as terpenoids. Shark liver oil contains a branched, unsaturated terpenoids known as squalene, 2,6,10,15,19,23-hexamethyl-2,6,10,14,18,22-tetracosahexaene, which is particularly preferred herein. Squalane, the saturated analog to squalene, is also a preferred oil. Fish oils, including squalene and squalane, are readily available from commercial sources or may be obtained by methods known in the art. Other preferred oils are the tocopherols (see below). Mixtures of oils can be used.

[0235] Surfactants can be classified by their 'HLB' (hydrophile/lipophile balance). Preferred surfactants of the invention have a HLB of at least 10, preferably at least 15, and more preferably at least 16. The invention can be used with surfactants including, but not limited to: the polyoxyethylene sorbitan esters surfactants (commonly referred to as the Tweens), especially polysorbate 20 and polysorbate 80; copolymers of ethylene oxide (EO), propylene oxide (PO), and/or butylene oxide (BO), sold under the DOWFAX™ tradename, such as linear EO/PO block copolymers; octoxynols, which can vary in the number of repeating ethoxy (oxy-1,2-ethanediyl) groups, with octoxynol-9 (Triton X-100, or t-octylphenoxypolyethoxyethanol) being of particular interest; (octylphenoxy)polyethoxyethanol (IGEPAL CA-630/NP-40); phospholipids such as phosphatidylcholine (lecithin); nonylphenol ethoxylates, such as the Tergitol™ NP series; polyoxyethylene fatty ethers derived from lauryl, cetyl, stearyl and oleyl alcohols (known as Brij surfactants), such as triethyleneglycol monolauryl ether (Brij 30); and sorbitan esters (commonly known as the SPANs), such as sorbitan trioleate (Span 85) and sorbitan monolaurate. Non-ionic surfactants are preferred. Preferred surfactants for including in the emulsion are Tween 80 (polyoxyethylene sorbitan monooleate), Span 85 (sorbitan trioleate), lecithin and Triton X-100.

[0236] Mixtures of surfactants can be used e.g. Tween 80/Span 85 mixtures. A combination of a polyoxyethylene sorbitan ester such as polyoxyethylene sorbitan monooleate (Tween 80) and an octoxynol such as t-octylphenoxypolyethoxyethanol (Triton X-100) is also suitable. Another useful combination comprises laureth 9 plus a polyoxyethylene sorbitan ester and/or an octoxynol.

[0237] Preferred amounts of surfactants (% by weight) are: polyoxyethylene sorbitan esters (such as Tween 80) 0.01 to 1%, in particular about 0.1 %; octyl- or nonylphenoxy polyoxyethanols (such as Triton X-100, or other detergents in the Triton series) 0.001 to 0.1 %, in particular 0.005 to 0.02%; polyoxyethylene ethers (such as laureth 9) 0.1 to 20 %, preferably 0.1 to 10% and in particular 0.1 to 1 % or about 0.5%.

[0238] Preferred emulsion adjuvants have an average droplets size of <1µm e.g. ≤750nm, ≤500nm, ≤400nm, ≤300nm, ≤250nm, ≤220nm, ≤200nm, or smaller. These droplet sizes can conveniently be achieved by techniques such as microfluidisation.

[0239] Specific oil-in-water emulsion adjuvants useful with the invention include, but are not limited to:

- A submicron emulsion of squalene, Tween 80, and Span 85. The composition of the emulsion by volume can be about 5% squalene, about 0.5% polysorbate 80 and about 0.5% Span 85. In weight terms, these ratios become 4.3% squalene, 0.5% polysorbate 80 and 0.48% Span 85. This adjuvant is known as 'MF59' [61-], as described in more detail in Chapter 10 of ref. 63 and chapter 12 of ref. 64. The MF59 emulsion advantageously includes citrate ions e.g. 10mM sodium citrate buffer.
- An emulsion of squalene, a tocopherol, and polysorbate 80 (Tween 80). The emulsion may include phosphate buffered saline. It may also include Span 85 (e.g. at 1%) and/or lecithin. These emulsions may have from 2 to 10% squalene, from 2 to 10% tocopherol and from 0.3 to 3% Tween 80, and the weight ratio of squalene:tocopherol is preferably ≤1 as this provides a more stable emulsion. Squalene and Tween 80 may be present volume ratio of about 5:2 or at a weight ratio of about 11:5. One such emulsion can be made by dissolving Tween 80 in PBS to give a 2% solution, then mixing 90ml of this solution with a mixture of (5g of DL-α-tocopherol and 5ml squalene), then microfluidising the mixture. The resulting emulsion may have submicron oil droplets e.g. with an average diameter of between 100 and 250nm, preferably about 180nm. The emulsion may also include a 3-de-O-acylated monophosphoryl lipid A (3d-MPL). Another useful emulsion of this type may comprise, per human dose, 0.5-10 mg squalene, 0.5-11 mg tocopherol, and 0.1-4 mg polysorbate 80 [65].
- An emulsion of squalene, a tocopherol, and a Triton detergent (e.g. Triton X-100). The emulsion may also include a 3d-MPL (see below). The emulsion may contain a phosphate buffer.
- An emulsion comprising a polysorbate (e.g. polysorbate 80), a Triton detergent (e.g. Triton X-100) and a tocopherol (e.g. an α-tocopherol succinate). The emulsion may include these three components at a mass ratio of about 75:11:10 (e.g. 750µg/ml polysorbate 80, 110µg/ml Triton X-100 and 100µg/ml α-tocopherol succinate), and these concentrations should include any contribution of these components from antigens. The emulsion may also include squalene. The emulsion may also include a 3d-MPL (see below). The aqueous phase may contain a phosphate buffer.

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- An emulsion of squalane, polysorbate 80 and poloxamer 401 ("Pluronic™ L121"), The emulsion can be formulated in phosphate buffered saline, pH 7.4. This emulsion is a useful delivery vehicle for muramyl dipeptides, and has been used with threonyl-MDP in the "SAF-1" adjuvant [66] (0.05-1% Thr-MDP, 5% squalane, 2.5% Pluronic L121 and 0.2% polysorbate 80). It can also be used without the Thr-MDP, as in the "AF" adjuvant [67] (5% squalane, 1.25% Pluronic L121 and 0.2% polysorbate 80). Microfluidisation is preferred.
- An emulsion comprising squalene, an aqueous solvent, a polyoxyethylene alkyl ether hydrophilic nonionic surfactant (e.g. polyoxyethylene (12) cetostearyl ether) and a hydrophobic nonionic surfactant (e.g. a sorbitan ester or mannide ester, such as sorbitan monoleate or 'Span 80'). The emulsion is preferably thermoreversible and/or has at least 90% of the oil droplets (by volume) with a size less than 200 nm [68]. The emulsion may also include one or more of: alditol; a cryoprotective agent (e.g. a sugar, such as dodecylmaltoside and/or sucrose); and/or an alkylpolyglycoside. The emulsion may include a TLR4 agonist [69]. Such emulsions may be lyophilized.
- An emulsion of squalene, poloxamer 105 and Abil-Care [70]. The final concentration (weight) of these components in adjuvanted vaccines are 5% squalene, 4% poloxamer 105 (pluronic polyol) and 2% Abil-Care 85 (Bis-PEG/PPG-16/16 PEG/PPG-16/16 dimethicone; caprylic/capric triglyceride).
- An emulsion having from 0.5-50% of an oil, 0.1-10% of a phospholipid, and 0.05-5% of a non-ionic surfactant. As described in reference 71, preferred phospholipid components are phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, phosphatidylglycerol, phosphatidic acid, sphingomyelin and cardiolipin. Submicron droplet sizes are advantageous.
- A submicron oil-in-water emulsion of a non-metabolizable oil (such as light mineral oil) and at least one surfactant (such as lecithin, Tween 80 or Span 80). Additives may be included, such as QuilA saponin, cholesterol, a saponin-lipophile conjugate (such as GPI-0100, described in reference 72, produced by addition of aliphatic amine to desacylsaponin via the carboxyl group of glucuronic acid), dimethyldioctadecylammonium bromide and/or N,N-dioctadecyl-N,N-bis (2-hydroxyethyl)propanediamine.
- An emulsion in which a saponin (e.g. QuilA or QS21) and a sterol (e.g. a cholesterol) are associated as helical micelles [73].
- An emulsion comprising a mineral oil, a non-ionic lipophilic ethoxylated fatty alcohol, and a non-ionic hydrophilic surfactant (e.g. an ethoxylated fatty alcohol and/or polyoxyethylene-polyoxypropylene block copolymer) [74].

[0240] In some embodiments an emulsion may be mixed with antigen extemporaneously, at the time of delivery, and thus the adjuvant and antigen may be kept separately in a packaged or distributed vaccine, ready for final formulation at the time of use. In other embodiments an emulsion is mixed with antigen during manufacture, and thus the composition is packaged in a liquid adjuvanted form. The antigen will generally be in an aqueous form, such that the vaccine is finally prepared by mixing two liquids. The volume ratio of the two liquids for mixing can vary (e.g. between 5:1 and 1:5) but is generally about 1:1. Where concentrations of components are given in the above descriptions of specific emulsions, these concentrations are typically for an undiluted composition, and the concentration after mixing with an antigen solution will thus decrease.

[0241] Where a composition includes a tocopherol, any of the α , β , γ , δ , ϵ or ξ tocopherols can be used, but α -tocopherols are preferred. The tocopherol can take several forms e.g. different salts and/or isomers. Salts include organic salts, such as succinate, acetate, nicotinate, etc. D- α -tocopherol and DL- α -tocopherol can both be used. Tocopherols are advantageously included in vaccines for use in elderly patients (e.g. aged 60 years or older) because vitamin E has been reported to have a positive effect on the immune response in this patient group [75]. They also have antioxidant properties that may help to stabilize the emulsions [76]. A preferred α -tocopherol is DL- α -tocopherol, and the preferred salt of this tocopherol is the succinate. The succinate salt has been found to cooperate with TNF-related ligands *in vivo*.

C. Saponin formulations

[0242] Saponin formulations may also be used as adjuvants in the invention. Saponins are a heterogeneous group of sterol glycosides and triterpenoid glycosides that are found in the bark, leaves, stems, roots and even flowers of a wide range of plant species. Saponin from the bark of the *Quillaia saponaria* Molina tree has been widely studied as adjuvant. Saponin can also be commercially obtained from *Smilax ornata* (sarsapilla), *Gypsophilla paniculata* (brides veil), and *Saponaria officinalis* (soap root). Saponin adjuvant formulations include purified formulations, such as QS21, as well as lipid formulations, such as ISCOMs. QS21 is marketed as Stimulon™.

[0243] Saponin compositions have been purified using HPLC and RP-HPLC. Specific purified fractions using these techniques have been identified, including QS7, QS17, QS18, QS21, QH-A, QH-B and QH-C. Preferably, the saponin is QS21. A method of production of QS21 is disclosed in ref. 77. Saponin formulations may also comprise a sterol, such as cholesterol [78].

[0244] Combinations of saponins and cholesterol can be used to form unique particles called immunostimulating complexes (ISCOMs) [chapter 23 of ref. 63]. ISCOMs typically also include a phospholipid such as phosphatidylethanolamine or phosphatidylcholine. Any known saponin can be used in ISCOMs. Preferably, the ISCOM includes one or more of QuilA, QHA & QHC. ISCOMs are further described in refs. 78-. Optionally, the ISCOMS may be devoid of additional detergent [80].

[0245] A review of the development of saponin based adjuvants can be found in ref. 81.

E. Bacterial or microbial derivatives

[0246] Adjuvants suitable for use in the invention include bacterial or microbial derivatives such as non-toxic derivatives of enterobacterial lipopolysaccharide (LPS), Lipid A derivatives, immunostimulatory oligonucleotides and ADP-ribosylating toxins and detoxified derivatives thereof.

[0247] Non-toxic derivatives of LPS include monophosphoryl lipid A (MPL) and 3-O-deacylated MPL (3dMPL). 3dMPL is a mixture of 3 de-O-acylated monophosphoryl lipid A with 4, 5 or 6 acylated chains. A preferred "small particle" form of 3 De-O-acylated monophosphoryl lipid A is disclosed in ref. 82. Such "small particles" of 3dMPL are small enough to be sterile filtered through a 0.22 μ m membrane [82]. Other non-toxic LPS derivatives include monophosphoryl lipid A mimics, such as aminoalkyl glucosaminide phosphate derivatives e.g. RC-529 [83].

[0248] Lipid A derivatives include derivatives of lipid A from *Escherichia coli* such as OM-174. OM-174 is described for example in refs. 84 & 85.

[0249] Immunostimulatory oligonucleotides suitable for use as adjuvants in the invention include nucleotide sequences containing a CpG motif (a dinucleotide sequence containing an unmethylated cytosine linked by a phosphate bond to a guanosine). Double-stranded RNAs and oligonucleotides containing palindromic or poly(dG) sequences have also been shown to be immunostimulatory.

[0250] The CpG's can include nucleotide modifications/analogs such as phosphorothioate modifications and can be double-stranded or single-stranded. References 86 and 87 disclose possible analog substitutions e.g. replacement of guanosine with 2'-deoxy-7-deazaguanosine. The adjuvant effect of CpG oligonucleotides is further discussed in refs. 88.

[0251] The CpG sequence may be directed to TLR9, such as the motif GTCGTT or TTCGTT [89]. The CpG sequence may be specific for inducing a Th1 immune response, such as a CpG-A ODN, or it may be more specific for inducing a B cell response, such a CpG-B ODN. CpG-A and CpG-B ODNs are discussed in refs. 90-. Preferably, the CpG is a CpG-A ODN.

[0252] Preferably, the CpG oligonucleotide is constructed so that the 5' end is accessible for receptor recognition. Optionally, two CpG oligonucleotide sequences may be attached at their 3' ends to form "immunomers". See, for example, refs. 92-.

[0253] A useful CpG adjuvant is CpG7909, also known as ProMune™ (Coley Pharmaceutical Group, Inc.). Another is CpG1826. As an alternative, or in addition, to using CpG sequences, TpG sequences can be used [94], and these oligonucleotides may be free from unmethylated CpG motifs. The immunostimulatory oligonucleotide may be pyrimidine-rich. For example, it may comprise more than one consecutive thymidine nucleotide (e.g. TTTT, as disclosed in ref. 94), and/or it may have a nucleotide composition with >25% thymidine (e.g. >35%, >40%, >50%, >60%, >80%, etc.). For example, it may comprise more than one consecutive cytosine nucleotide (e.g. CCCC, as disclosed in ref. 94), and/or it may have a nucleotide composition with >25% cytosine (e.g. >35%, >40%, >50%, >60%, >80%, etc.). These oligonucleotides may be free from unmethylated CpG motifs. Immunostimulatory oligonucleotides will typically comprise at least 20 nucleotides. They may comprise fewer than 100 nucleotides.

[0254] A particularly useful adjuvant based around immunostimulatory oligonucleotides is known as IC-31™ [95]. Thus an adjuvant used with the invention may comprise a mixture of (i) an oligonucleotide (e.g. between 15-40 nucleotides) including at least one (and preferably multiple) Cpl motifs (i.e. a cytosine linked to an inosine to form a dinucleotide), and (ii) a polycationic polymer, such as an oligopeptide (e.g. between 5-20 amino acids) including at least one (and preferably multiple) Lys-Arg-Lys tripeptide sequence(s). The oligonucleotide may be a deoxynucleotide comprising 26-mer sequence 5'-(IC)₃₁-3'.

[0255] Bacterial ADP-ribosylating toxins and detoxified derivatives thereof may be used as adjuvants in the invention. Preferably, the protein is derived from *E.coli* (*E.coli* heat labile enterotoxin "LT"), cholera ("CT"), or pertussis ("PT"). The use of detoxified ADP-ribosylating toxins as mucosal adjuvants is described in ref. 96 and as parenteral adjuvants in ref. 97. The toxin or toxoid is preferably in the form of a holotoxin, comprising both A and B subunits. Preferably, the A subunit contains a detoxifying mutation; preferably the B subunit is not mutated. Preferably, the adjuvant is a detoxified LT mutant such as LT-K63, LT-R72, and LT-G192. The use of ADP-ribosylating toxins and detoxified derivatives thereof,

particularly LT-K63 and LT-R72, as adjuvants can be found in refs. 98-101. A useful CT mutant is or CT-E29H [102]. Numerical reference for amino acid substitutions is preferably based on the alignments of the A and B subunits of ADP-ribosylating toxins set forth in ref. 103, specifically incorporated herein by reference in its entirety.

5 *F. Human immunomodulators*

[0256] Human immunomodulators suitable for use as adjuvants in the invention include cytokines, such as interleukins (e.g. IL-1, IL-2, IL-4, IL-5, IL-6, IL-7, IL-12 [104], etc.), interferons (e.g. interferon- γ), macrophage colony stimulating factor, and tumor necrosis factor. A preferred immunomodulator is IL-12.

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G. Bioadhesives and Mucoadhesives

[0257] Bioadhesives and mucoadhesives may also be used as adjuvants in the invention. Suitable bioadhesives include esterified hyaluronic acid microspheres [105] or mucoadhesives such as cross-linked derivatives of poly(acrylic acid), polyvinyl alcohol, polyvinyl pyrrolidone, polysaccharides and carboxymethylcellulose. Chitosan and derivatives thereof may also be used as adjuvants in the invention [106].

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H. Microparticles

[0258] Microparticles may also be used as adjuvants in the invention. Microparticles (*i.e.* a particle of ~100nm to ~150 μ m in diameter, more preferably ~200nm to ~30 μ m in diameter, and most preferably ~500nm to ~10 μ m in diameter) formed from materials that are biodegradable and non-toxic (e.g. a poly(α -hydroxy acid), a polyhydroxybutyric acid, a polyorthoester, a polyanhydride, a polycaprolactone, etc.), with poly(lactide-co-glycolide) are preferred, optionally treated to have a negatively-charged surface (e.g. with SDS) or a positively-charged surface (e.g. with a cationic detergent, such as CTAB).

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I. Liposomes

[0259] Examples of liposome formulations suitable for use as adjuvants are described in refs. 107-.

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J. Polyoxyethylene ether and polyoxyethylene ester formulations

[0260] Adjuvants suitable for use in the invention include polyoxyethylene ethers and polyoxyethylene esters [109]. Such formulations further include polyoxyethylene sorbitan ester surfactants in combination with an octoxynol [110] as well as polyoxyethylene alkyl ethers or ester surfactants in combination with at least one additional non-ionic surfactant such as an octoxynol [111]. Preferred polyoxyethylene ethers are selected from the following group: polyoxyethylene-9-lauryl ether (laureth 9), polyoxyethylene-9-stearyl ether, polyoxyethylene-8-stearyl ether, polyoxyethylene-4-lauryl ether, polyoxyethylene-35-lauryl ether, and polyoxyethylene-23-lauryl ether.

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K. Phosphazenes

[0261] A phosphazene, such as poly[di(carboxylatophenoxy)phosphazene] ("PCPP") as described, for example, in references 112 and 113, may be used.

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L. Muramyl peptides

[0262] Examples of muramyl peptides suitable for use as adjuvants in the invention include N-acetyl-muramyl-L-threonyl-D-isoglutamine (thr-MDP), N-acetyl-normuramyl-L-alanyl-D-isoglutamine (nor-MDP), and N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-*sn*-glycero-3-hydroxyphosphoryloxy)-ethylamine MTP-PE).

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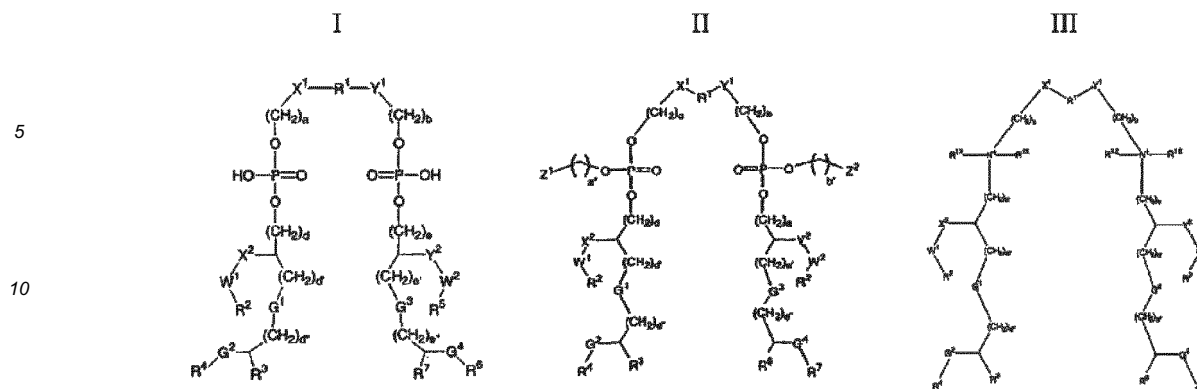
M. Imidazoquinolone Compounds.

[0263] Examples of imidazoquinolone compounds suitable for use adjuvants in the invention include Imiquimod ("R-837") [114], Resiquimod ("R-848") [115], and their analogs; and salts thereof (e.g. the hydrochloride salts).

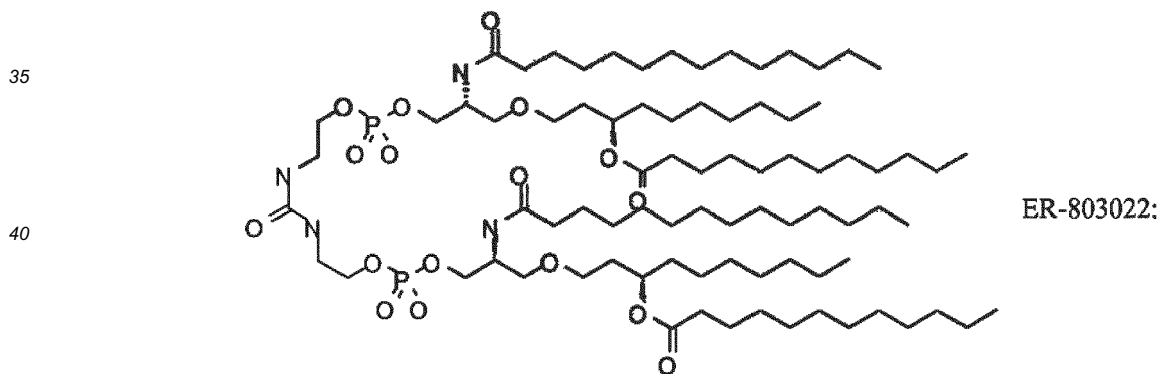
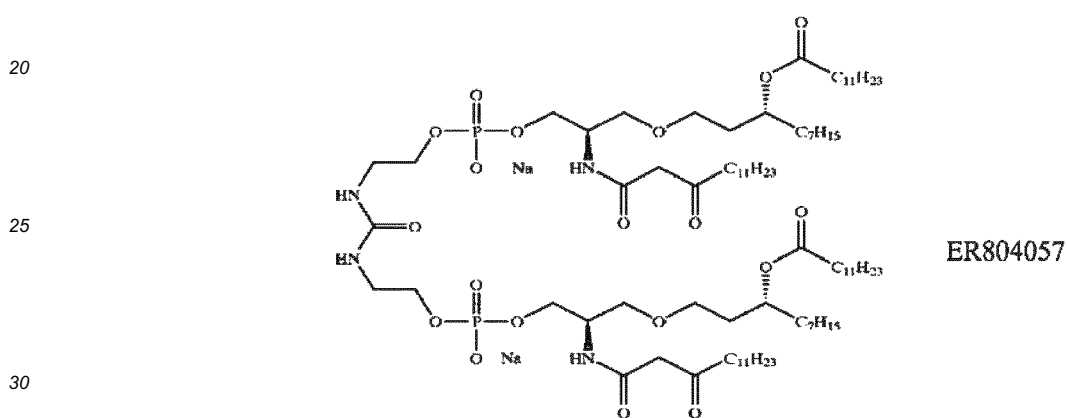
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N. Substituted ureas

[0264] Substituted ureas useful as adjuvants include compounds of formula I, II or III, or salts thereof:



as defined in reference 116, such as 'ER 803058', 'ER 803732', 'ER 804053', ER 804058', 'ER 804059', 'ER 804442', 'ER 804680', 'ER 804764', ER 803022 or 'ER 804057' e.g.:



O. Further adjuvants

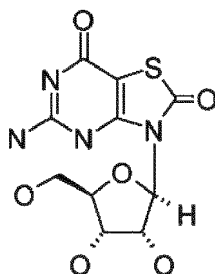
[0265] Further adjuvants that may be used with the invention include:

- An aminoalkyl glucosaminide phosphate derivative, such as RC-529 [117].
- A thiosemicarbazone compound, such as those disclosed in reference 118. Methods of formulating, manufacturing, and screening for active compounds are also described in reference 118. The thiosemicarbazones are particularly effective in the stimulation of human peripheral blood mononuclear cells for the production of cytokines, such as TNF- α .
- A tryptanthrin compound, such as those disclosed in reference 119. Methods of formulating, manufacturing, and screening for active compounds are also described in reference 119. The thiosemicarbazones are particularly

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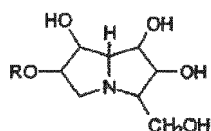
effective in the stimulation of human peripheral blood mononuclear cells for the production of cytokines, such as TNF- α .

- A nucleoside analog, such as: (a) Isatorabine (ANA-245; 7-thia-8-oxoguanosine):



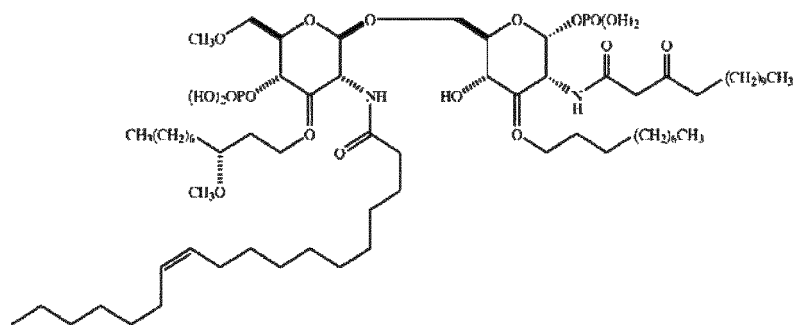
and prodrugs thereof; (b) ANA975; (c) ANA-025-1; (d) ANA380; (e) the compounds disclosed in references 120 to Loxoribine (7-allyl-8-oxoguanosine) [122].

- Compounds disclosed in reference 123, including: Acylpiperazine compounds, Indoleione compounds, Tetrahydroisoquinoline (THIQ) compounds, Benzocyclodione compounds, Aminoazavinyl compounds, Aminobenzimidazole quinolinone (ABIQ) compounds [124], Hydraphtalamide compounds, Benzophenone compounds, Isoxazole compounds, Sterol compounds, Quinazolinone compounds, Pyrrole compounds [125], Anthraquinone compounds, Quinoxaline compounds, Triazine compounds, Pyrazalopyrimidine compounds, and Benzazole compounds [126].
- Compounds containing lipids linked to a phosphate-containing acyclic backbone, such as the TLR4 antagonist E5564 [127].
- A polyoxidonium polymer [128] or other N-oxidized polyethylene-piperazine derivative.
- Methyl inosine 5'-monophosphate ("MIMP") [129].
- A polyhydroxylated pyrrolizidine compound [130], such as one having formula:



where R is selected from the group comprising hydrogen, straight or branched, unsubstituted or substituted, saturated or unsaturated acyl, alkyl (e.g. cycloalkyl), alkenyl, alkynyl and aryl groups, or a pharmaceutically acceptable salt or derivative thereof. Examples include, but are not limited to: casuarine, casuarine-6- α -D-glucopyranose, 3-*epi*-casuarine, 7-*epi*-casuarine, 3,7-*diepi*-casuarine, etc.

- A CD1d ligand, such as an α -glycosylceramide [131-] (e.g. α -galactosylceramide), phytosphingosine-containing α -glycosylceramides, OCH, KRN7000 [(2S,3S,4R)-1-O-(α -D-galactopyranosyl)-2-(N-hexacosanoylamino)-1,3,4-octadecanetriol], CRONY-101, 3"-O-sulfogalactosylceramide, etc.
- A gamma inulin [133] or derivative thereof, such as algammulin.

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Adjuvant combinations

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[0266] The invention may also comprise combinations of one or more of the adjuvants identified above. For example, the following adjuvant compositions may be used in the invention: (1) a saponin and an oil-in-water emulsion [134]; (2) a saponin (e.g. QS21) + a non-toxic LPS derivative (e.g. 3dMPL); (3) a saponin (e.g. QS21) + a non-toxic LPS derivative (e.g. 3dMPL) + a cholesterol; (4) a saponin (e.g. QS21) + 3dMPL + IL-12 (optionally + a sterol); (5) combinations of 3dMPL with, for example, QS21 and/or oil-in-water emulsions [135]; (6) SAF, containing 10% squalane, 0.4% Tween 80™, 5% pluronic-block polymer L121, and thr-MDP, either microfluidized into a submicron emulsion or vortexed to generate a larger particle size emulsion. (7) Ribi™ adjuvant system (RAS), (Ribi Immunochem) containing 2% squalene, 0.2% Tween 80, and one or more bacterial cell wall components from the group consisting of monophosphorylipid A (MPL), trehalose dimycolate (TDM), and cell wall skeleton (CWS), preferably MPL + CWS (Detox™); and (8) one or more mineral salts (such as an aluminum salt) + a non-toxic derivative of LPS (such as 3dMPL).

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[0267] The use of an aluminium hydroxide and/or aluminium phosphate adjuvant is particularly preferred, and antigens are generally adsorbed to these salts. Calcium phosphate is another preferred adjuvant. Other preferred adjuvant combinations include combinations of Th1 and Th2 adjuvants such as CpG & alum or resiquimod & alum. A combination of aluminium phosphate and 3dMPL may be used.

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[0268] The compositions of the invention may elicit both a cell mediated immune response as well as a humoral immune response. This immune response will preferably induce long lasting (e.g. neutralising) antibodies and a cell mediated immunity that can quickly respond upon exposure to pseudomonas.

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[0269] Two types of T cells, CD4 and CD8 cells, are generally thought necessary to initiate and/or enhance cell mediated immunity and humoral immunity. CD8 T cells can express a CD8 co-receptor and are commonly referred to as Cytotoxic T lymphocytes (CTLs). CD8 T cells are able to recognized or interact with antigens displayed on MHC Class I molecules.

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[0270] CD4 T cells can express a CD4 co-receptor and are commonly referred to as T helper cells. CD4 T cells are able to recognize antigenic peptides bound to MHC class II molecules. Upon interaction with a MHC class II molecule, the CD4 cells can secrete factors such as cytokines. These secreted cytokines can activate B cells, cytotoxic T cells, macrophages, and other cells that participate in an immune response. Helper T cells or CD4+ cells can be further divided into two functionally distinct subsets: TH1 phenotype and TH2 phenotypes which differ in their cytokine and effector function.

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[0271] Activated TH1 cells enhance cellular immunity (including an increase in antigen-specific CTL production) and are therefore of particular value in responding to intracellular infections. Activated TH1 cells may secrete one or more of IL-2, IFN- γ , and TNF- β . A TH1 immune response may result in local inflammatory reactions by activating macrophages, NK (natural killer) cells, and CD8 cytotoxic T cells (CTLs). A TH1 immune response may also act to expand the immune response by stimulating growth of B and T cells with IL-12. TH1 stimulated B cells may secrete IgG2a.

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[0272] Activated TH2 cells enhance antibody production and are therefore of value in responding to extracellular infections. Activated TH2 cells may secrete one or more of IL-4, IL-5, IL-6, and IL-10. A TH2 immune response may result in the production of IgG1, IgE, IgA and memory B cells for future protection.

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[0273] An enhanced immune response may include one or more of an enhanced TH1 immune response and a TH2 immune response.

[0274] A TH1 immune response may include one or more of an increase in CTLs, an increase in one or more of the cytokines associated with a TH1 immune response (such as IL-2, IFN- γ , and TNF- β), an increase in activated macrophages, an increase in NK activity, or an increase in the production of IgG2a. Preferably, the enhanced TH1 immune response will include an increase in IgG2a production.

[0275] A TH1 immune response may be elicited using a TH1 adjuvant. A TH1 adjuvant will generally elicit increased levels of IgG2a production relative to immunization of the antigen without adjuvant. TH1 adjuvants suitable for use in the invention may include for example saponin formulations, virosomes and virus like particles, non-toxic derivatives of

enterobacterial lipopolysaccharide (LPS), immunostimulatory oligonucleotides. Immunostimulatory oligonucleotides, such as oligonucleotides containing a CpG motif, are preferred TH1 adjuvants for use in the invention.

[0276] A TH2 immune response may include one or more of an increase in one or more of the cytokines associated with a TH2 immune response (such as IL-4, IL-5, IL-6 and IL-10), or an increase in the production of IgG1, IgE, IgA and memory B cells. Preferably, the enhanced TH2 immune response will include an increase in IgG1 production.

[0277] A TH2 immune response may be elicited using a TH2 adjuvant. A TH2 adjuvant will generally elicit increased levels of IgG1 production relative to immunization of the antigen without adjuvant. TH2 adjuvants suitable for use in the invention include, for example, mineral containing compositions, oil-emulsions, and ADP-ribosylating toxins and detoxified derivatives thereof. Mineral containing compositions, such as aluminium salts are preferred TH2 adjuvants for use in the invention.

[0278] Preferably, the invention includes a composition comprising a combination of a TH1 adjuvant and a TH2 adjuvant. Preferably, such a composition elicits an enhanced TH1 and an enhanced TH2 response, i.e., an increase in the production of both IgG1 and IgG2a production relative to immunization without an adjuvant. Still more preferably, the composition comprising a combination of a TH1 and a TH2 adjuvant elicits an increased TH1 and/or an increased TH2 immune response relative to immunization with a single adjuvant (i.e., relative to immunization with a TH1 adjuvant alone or immunization with a TH2 adjuvant alone).

[0279] The immune response may be one or both of a TH1 immune response and a TH2 response. Preferably, immune response provides for one or both of an enhanced TH1 response and an enhanced TH2 response.

[0280] The enhanced immune response may be one or both of a systemic and a mucosal immune response. Preferably, the immune response provides for one or both of an enhanced systemic and an enhanced mucosal immune response. Preferably the mucosal immune response is a TH2 immune response. Preferably, the mucosal immune response includes an increase in the production of IgA.

[0281] *P. aeruginosa* infections can affect various areas of the body and so the compositions of the invention may be prepared in various forms. For example, the compositions may be prepared as injectables, either as liquid solutions or suspensions. Solid forms suitable for solution in, or suspension in, liquid vehicles prior to injection can also be prepared (e.g. a lyophilised composition or a spray-freeze dried composition). The composition may be prepared for topical administration e.g. as an ointment, cream or powder. The composition may be prepared for oral administration e.g. as a tablet or capsule, as a spray, or as a syrup (optionally flavoured). The composition may be prepared for pulmonary administration e.g. as an inhaler, using a fine powder or a spray. The composition may be prepared as a suppository or pessary. The composition may be prepared for nasal, aural or ocular administration e.g. as drops. The composition may be in kit form, designed such that a combined composition is reconstituted just prior to administration to a patient. Such kits may comprise one or more antigens in liquid form and one or more lyophilised antigens.

[0282] Where a composition is to be prepared extemporaneously prior to use (e.g. where a component is presented in lyophilised form) and is presented as a kit, the kit may comprise two vials, or it may comprise one ready-filled syringe and one vial, with the contents of the syringe being used to reactivate the contents of the vial prior to injection.

[0283] Immunogenic compositions used as vaccines comprise an immunologically effective amount of antigen(s), as well as any other components, as needed. By 'immunologically effective amount', it is meant that the administration of that amount to an individual, either in a single dose or as part of a series, is effective for treatment or prevention. This amount varies depending upon the health and physical condition of the individual to be treated, age, the taxonomic group of individual to be treated (e.g. non-human primate, primate, etc.), the capacity of the individual's immune system to synthesise antibodies, the degree of protection desired, the formulation of the vaccine, the treating doctor's assessment of the medical situation, and other relevant factors. It is expected that the amount will fall in a relatively broad range that can be determined through routine trials. Where more than one antigen is included in a composition then two antigens may be present at the same dose as each other or at different doses.

[0284] As mentioned above, a composition may include a temperature protective agent, and this component may be particularly useful in adjuvanted compositions (particularly those containing a mineral adjuvant, such as an aluminium salt). As described in reference 136, a liquid temperature protective agent may be added to an aqueous vaccine composition to lower its freezing point e.g. to reduce the freezing point to below 0°C. Thus the composition can be stored below 0°C, but above its freezing point, to inhibit thermal breakdown. The temperature protective agent also permits freezing of the composition while protecting mineral salt adjuvants against agglomeration or sedimentation after freezing and thawing, and may also protect the composition at elevated temperatures e.g. above 40°C. A starting aqueous vaccine and the liquid temperature protective agent may be mixed such that the liquid temperature protective agent forms from 1-80% by volume of the final mixture. Suitable temperature protective agents should be safe for human administration, readily miscible/soluble in water, and should not damage other components (e.g. antigen and adjuvant) in the composition. Examples include glycerin, propylene glycol, and/or polyethylene glycol (PEG). Suitable PEGs may have an average molecular weight ranging from 200-20,000 Da. In a preferred embodiment, the polyethylene glycol can have an average molecular weight of about 300 Da ('PEG-300').

[0285] The invention provides an immunogenic composition comprising: (i) one or more antigen(s) selected from the

first, second, third or fourth antigen groups; and (ii) a temperature protective agent. This composition may be formed by mixing (i) an aqueous composition comprising one or more antigen(s) selected from the first, second, third or fourth antigen groups, with (ii) a temperature protective agent. The mixture may then be stored e.g. below 0°C, from 0-20°C, from 20-35°C, from 35-55°C, or higher. It may be stored in liquid or frozen form. The mixture may be lyophilised. The composition may alternatively be formed by mixing (i) a dried composition comprising one or more antigen(s) selected from the first, second, third or fourth antigen groups, with (ii) a liquid composition comprising the temperature protective agent. Thus component (ii) can be used to reconstitute component (i).

Methods of treatment, and administration of the vaccine

[0286] The invention also provides a method for raising an immune response in a mammal comprising the step of administering an effective amount of a composition of the invention. The immune response is preferably protective and preferably involves antibodies and/or cell-mediated immunity. The method may raise a booster response.

[0287] The invention also provides at least two antigens of the invention for combined use as a medicament e.g. for use in raising an immune response in a mammal.

[0288] The invention also provides the use of at least two antigens of the invention in the manufacture of a medicament for raising an immune response in a mammal.

[0289] By raising an immune response in the mammal by these uses and methods, the mammal can be protected against *P. aeruginosa* infection, including a nosocomial infection. More particularly, the mammal may be protected against a skin infection, including those of burns, trauma wounds and the eyes as shown in reference 137. pneumonia, meningitis and neonatal meningitis, osteomyelitis endocarditis, pseudomonas folliculitis, toxic shock syndrome, and/or septicaemia and cystic fibrosis.

[0290] The invention also provides a kit comprising a first component and a second component wherein neither the first component nor the second component is a composition of the invention as described above, but wherein the first component and the second component can be combined to provide a composition of the invention as described above. The kit may further include a third component comprising one or more of the following: instructions, syringe or other delivery device, adjuvant, or pharmaceutically acceptable formulating solution.

[0291] The invention also provides a delivery device pre-filled with an immunogenic composition of the invention.

[0292] The mammal is preferably a human. Where the vaccine is for prophylactic use, the human is preferably a child (e.g. a toddler or infant) or a teenager; where the vaccine is for therapeutic use, the human is preferably a teenager or an adult. A vaccine intended for children may also be administered to adults e.g. to assess safety, dosage, immunogenicity, etc. Other mammals which can usefully be immunised according to the invention are cows, dogs, horses, and pigs.

[0293] One way of checking efficacy of therapeutic treatment involves monitoring *P. aeruginosa* infection after administration of the compositions of the invention. One way of checking efficacy of prophylactic treatment involves monitoring immune responses, systemically (such as monitoring the level of IgG1 and IgG2a production) and/or mucosally (such as monitoring the level of IgA production), against the antigens in the compositions of the invention after administration of the composition. Typically, antigen-specific serum antibody responses are determined post-immunisation but pre-challenge whereas antigen-specific mucosal antibody responses are determined post-immunisation and post-challenge.

[0294] Another way of assessing the immunogenicity of the compositions of the present invention is to express the proteins recombinantly for screening patient sera or mucosal secretions by immunoblot and/or microarrays. A positive reaction between the protein and the patient sample indicates that the patient has mounted an immune response to the protein in question. This method may also be used to identify immunodominant antigens and/or epitopes within antigens.

[0295] The efficacy of vaccine compositions can also be determined *in vivo* by challenging animal models of *P. aeruginosa* infection, e.g., guinea pigs or mice, with the vaccine compositions. In particular, there one useful animal model for the study of *P. aeruginosa* infectious disease, described in details in the chapter entitled "efficacy testing" The lethal infection model looks at the number of mice which survive after being infected by a normally-lethal dose of *P. aeruginosa* via intra-tracheal route. Different antigens, and different antigen combinations, may contribute to different aspects of an effective vaccine.

[0296] Compositions of the invention will generally be administered directly to a patient. Direct delivery may be accomplished by parenteral injection (e.g. subcutaneously, intraperitoneally, intravenously, intramuscularly, or to the interstitial space of a tissue), or mucosally, such as by rectal, oral (e.g. *tablet*, spray), vaginal, topical, transdermal or transcutaneous, intranasal, ocular, aural, pulmonary or other mucosal administration.

[0297] The invention may be used to elicit systemic and/or mucosal immunity, preferably to elicit an enhanced systemic and/or mucosal immunity.

[0298] Preferably the enhanced systemic and/or mucosal immunity is reflected in an enhanced TH1 and/or TH2 immune response. Preferably, the enhanced immune response includes an increase in the production of IgG1 and/or IgG2a and/or IgA.

[0299] Th17 cells are a recently described lineage of helper T cells that can enhance antibacterial mucosal defenses

and can potentially mediate protective vaccine-induced response. See reference 138

[0300] Dosage can be by a single dose schedule or a multiple dose schedule. Multiple doses may be used in a primary immunisation schedule and/or in a booster immunisation schedule. In a multiple dose schedule the various doses may be given by the same or different routes *e.g.* a parenteral prime and mucosal boost, a mucosal prime and parenteral boost, *etc.* Multiple doses will typically be administered at least 1 week apart (*e.g.* about 2 weeks, about 3 weeks, about 4 weeks, about 6 weeks, about 8 weeks, about 10 weeks, about 12 weeks, about 16 weeks, *etc.*).

[0301] Vaccines prepared according to the invention may be used to treat both children and adults. Thus a human patient may be less than 1 year old, 1-5 years old, 5-15 years old, 15-55 years old, or at least 55 years old. Preferred patients for receiving the vaccines are the elderly (*e.g.* ≥ 50 years old, ≥ 60 years old, and preferably ≥ 65 years), the young (*e.g.* ≤ 5 years old), hospitalised patients, healthcare workers, armed service and military personnel, pregnant women, the chronically ill, or immunodeficient patients. The vaccines are not suitable solely for these groups, however, and may be used more generally in a population.

[0302] Vaccines produced by the invention may be administered to patients at substantially the same time as (*e.g.* during the same medical consultation or visit to a healthcare professional or vaccination centre) other vaccines *e.g.* at substantially the same time as an influenza vaccine, a measles vaccine, a mumps vaccine, a rubella vaccine, a MMR vaccine, a varicella vaccine, a MMRV vaccine, a diphtheria vaccine, a tetanus vaccine, a pertussis vaccine, a DTP vaccine, a conjugated *H.influenzae* type b vaccine, an inactivated poliovirus vaccine, a hepatitis B virus vaccine, a meningococcal conjugate vaccine (such as a tetravalent A-C-W135-Y vaccine), a respiratory syncytial virus vaccine, *etc.* Further non-pseudomonas vaccines suitable for co-administration may include one or more antigens.

Nucleic acid immunisation

[0303] The immunogenic compositions described above include polypeptide antigens from *P. aeruginosa*. In all cases, however, the polypeptide antigens can be replaced by nucleic acids (typically DNA) encoding those polypeptides, to give compositions, methods and uses based on nucleic acid immunisation. Nucleic acid immunisation is now a developed field.

[0304] The nucleic acid encoding the immunogen is expressed *in vivo* after delivery to a patient and the expressed immunogen then stimulates the immune system. The active ingredient will typically take the form of a nucleic acid vector comprising: (i) a promoter; (ii) a sequence encoding the immunogen, operably linked to the promoter; and optionally (iii) a selectable marker. Preferred vectors may further comprise (iv) an origin of replication; and (v) a transcription terminator downstream of and operably linked to (ii). In general, (i) & (v) will be eukaryotic and (iii) & (iv) will be prokaryotic.

[0305] Preferred promoters are viral promoters *e.g.* from cytomegalovirus (CMV). The vector may also include transcriptional regulatory sequences (*e.g.* enhancers) in addition to the promoter and which interact functionally with the promoter. Preferred vectors include the immediate-early CMV enhancer/promoter, and more preferred vectors also include CMV intron A. The promoter is operably linked to a downstream sequence encoding an immunogen, such that expression of the immunogen-encoding sequence is under the promoter's control.

[0306] Where a marker is used, it preferably functions in a microbial host (*e.g.* in a prokaryote, in a bacteria, in a yeast). The marker is preferably a prokaryotic selectable marker (*e.g.* transcribed under the control of a prokaryotic promoter). For convenience, typical markers are antibiotic resistance genes.

[0307] The vector of the invention is preferably an autonomously replicating episomal or extrachromosomal vector, such as a plasmid.

[0308] The vector of the invention preferably comprises an origin of replication. It is preferred that the origin of replication is active in prokaryotes but not in eukaryotes.

[0309] Preferred vectors thus include a prokaryotic marker for selection of the vector, a prokaryotic origin of replication, but a eukaryotic promoter for driving transcription of the immunogen-encoding sequence. The vectors will therefore (a) be amplified and selected in prokaryotic hosts without polypeptide expression, but (b) be expressed in eukaryotic hosts without being amplified. This arrangement is ideal for nucleic acid immunization vectors.

[0310] The vector of the invention may comprise a eukaryotic transcriptional terminator sequence downstream of the coding sequence. This can enhance transcription levels. Where the coding sequence does not have its own, the vector of the invention preferably comprises a polyadenylation sequence. A preferred polyadenylation sequence is from bovine growth hormone.

[0311] The vector of the invention may comprise a multiple cloning site

[0312] In addition to sequences encoding the immunogen and a marker, the vector may comprise a second eukaryotic coding sequence. The vector may also comprise an IRES upstream of said second sequence in order to permit translation of a second eukaryotic polypeptide from the same transcript as the immunogen. Alternatively, the immunogen-coding sequence may be downstream of an IRES.

[0313] The vector of the invention may comprise unmethylated CpG motifs *e.g.* unmethylated DNA sequences which have in common a cytosine preceding a guanosine, flanked by two 5' purines and two 3' pyrimidines. In their unmethylated

form these DNA motifs have been demonstrated to be potent stimulators of several types of immune cell.

[0314] Vectors may be delivered in a targeted way. Receptor-mediated DNA delivery techniques are described in the known art. Therapeutic compositions containing a nucleic acid are administered in a range of about 100ng to about 200mg of DNA for local administration in a gene therapy protocol. Concentration ranges of about 500 ng to about 50 mg, about 1 μ g to about 2 mg, about 5 μ g to about 500 μ g, and about 20 μ g to about 100 μ g of DNA can also be used during a gene therapy protocol. Factors such as method of action (e.g. for enhancing or inhibiting levels of the encoded gene product) and efficacy of transformation and expression are considerations which will affect the dosage required for ultimate efficacy. Where greater expression is desired over a larger area of tissue, larger amounts of vector or the same amounts re-administered in a successive protocol of administrations, or several administrations to different adjacent or close tissue portions may be required to effect a positive therapeutic outcome. In all cases, routine experimentation in clinical trials will determine specific ranges for optimal therapeutic effect.

[0315] Vectors can be delivered using gene delivery vehicles. The gene delivery vehicle can be of viral or non-viral origin (see generally reference 139).

[0316] Viral-based vectors for delivery of a desired nucleic acid and expression in a desired cell are well known in the art. Exemplary viral-based vehicles include, but are not limited to, recombinant retroviruses (e.g. references 140 to), alphavirus-based vectors (e.g. Sindbis virus vectors, Semliki forest virus (ATCC VR-67; ATCC VR-1247), Ross River virus (ATCC VR-373; ATCC VR-1246) and Venezuelan equine encephalitis virus (ATCC VR-923; ATCC VR-1250; ATCC VR 1249; ATCC VR-532); hybrids or chimeras of these viruses may also be used), poxvirus vectors (e.g. vaccinia, fowlpox, canarypox, modified vaccinia Ankara, etc.), adenovirus vectors, and adeno-associated virus (AAV) vectors (e.g. see refs. 142 to). Administration of DNA linked to killed adenovirus [144] can also be employed.

[0317] Non-viral delivery vehicles and methods can also be employed, including, but not limited to, polycationic condensed DNA linked or unlinked to killed adenovirus alone [e.g. 144], ligand-linked DNA [145], eukaryotic cell delivery vehicles cells [e.g. refs. 146 to] and nucleic charge neutralization or fusion with cell membranes. Naked DNA can also be employed. Exemplary naked DNA introduction methods are described in ref. 148. Liposomes (e.g. immunoliposomes) that can act as gene delivery vehicles are described in refs. 149 to. Additional approaches are described in references 151-152.

[0318] Further non-viral delivery suitable for use includes mechanical delivery systems such as the approach described in ref. 152. Moreover, the coding sequence and the product of expression of such can be delivered through deposition of photopolymerized hydrogel materials or use of ionizing radiation (e.g. refs. 153). Other conventional methods for gene delivery that can be used for delivery of the coding sequence include, for example, use of hand-held gene transfer particle gun [154] or use of ionizing radiation for activating transferred genes.

[0319] Delivery DNA using PLG {poly(lactide-co-glycolide)} microparticles is a particularly preferred method e.g. by adsorption to the microparticles, which are optionally treated to have a negatively-charged surface (e.g. treated with SDS) or a positively-charged surface (e.g. treated with a cationic detergent, such as CTAB).

Antibodies

[0320] Antibodies against *P. aeruginosa* antigens can be used for passive immunisation. Thus the invention provides an antibody which is specific for an antigen in the first, second, third or fourth antigen groups. The invention also provides the use of such antibodies in therapy. The invention also provides the use of such antibodies in the manufacture of a medicament. The invention also provides a method for treating a mammal comprising the step of administering an effective amount of an antibody of the invention. As described above for immunogenic compositions, these methods and uses allow a mammal to be protected against *P. aeruginosa* infection.

[0321] The term "antibody" includes intact immunoglobulin molecules, as well as fragments thereof which are capable of binding an antigen. These include hybrid (chimeric) antibody molecules; F(ab')₂ and F(ab) fragments and Fv molecules; non-covalent heterodimers; single-chain Fv molecules (sFv); dimeric and trimeric antibody fragment constructs; minibodies; humanized antibody molecules; and any functional fragments obtained from such molecules, as well as antibodies obtained through non-conventional processes such as phage display. Preferably, the antibodies are monoclonal antibodies. Methods of obtaining monoclonal antibodies are well known in the art. Humanised or fully-human antibodies are preferred.

General

[0322] The practice of the present invention will employ, unless otherwise indicated, conventional methods of chemistry, biochemistry, molecular biology, immunology and pharmacology, within the skill of the art. Such techniques are explained fully in the literature.

[0323] "GI" numbering is used above. A GI number, or "GenInfo Identifier", is a series of digits assigned consecutively to each sequence record processed by NCBI when sequences are added to its databases. The GI number bears no

resemblance to the accession number of the sequence record. When a sequence is updated (e.g. for correction, or to add more annotation or information) then it receives a new GI number. Thus the sequence associated with a given GI number is never changed. See also reference 37.

[0324] Where the invention concerns an "epitope", this epitope may be a B-cell epitope and/or a T-cell epitope. Such epitopes can be identified empirically (e.g. using PEPSCAN [155] or similar methods), or they can be predicted (e.g. using the Jameson-Wolf antigenic index [156], matrix-based approaches [157], MAPITOPE [158], TEPITOPE [159], OptiMer & EpiMer [160], ADEPT [161], Tsites, hydrophilicity, antigenic index or the methods known in the art. Epitopes are the parts of an antigen that are recognised by and bind to the antigen binding sites of antibodies or T-cell receptors, and they may also be referred to as "antigenic determinants".

[0325] Where an antigen "domain" is omitted, this may involve omission of a signal peptide, of a cytoplasmic domain, of a transmembrane domain, of an extracellular domain, etc.

[0326] The term "comprising" encompasses "including" as well as "consisting" e.g. a composition "comprising" X may consist exclusively of X or may include something additional e.g. X + Y.

[0327] The term "about" in relation to a numerical value x is optional and means, for example, $x \pm 10\%$.

[0328] References to a percentage sequence identity between two amino acid sequences means that, when aligned, that percentage of amino acids are the same in comparing the two sequences. This alignment and the percent homology or sequence identity can be determined using software programs known in the art, for example those described in section 7.7.18 of ref. 162. A preferred alignment is determined by the Smith-Waterman homology search algorithm using an affine gap search with a gap open penalty of 12 and a gap extension penalty of 2, BLOSUM matrix of 62. The Smith-Waterman homology search algorithm is disclosed in ref. 163.

MODES FOR CARRYING OUT THE INVENTION

Antigen selection

[0329] *P. aeruginosa* proteins have been selected for use as vaccine components based on the combination of various criteria which include the following ones:

- Cellular localization prediction, through which priority was attributed to proteins predicted as "outer membrane", "periplasmic", extracellular" and "unknown". In relation to the latest definition proteins predicted as having an "unknown" cellular localization which are often composed of multiple domains, of which one could actually be surface exposed.
- Significant homology to known virulence factors, vaccine candidates from other species
- Lack of significant homology to human proteins encoded by the sequenced human genome, in order to limit the probability of generation of autoimmune response or vaccine induced autoimmunity.
- Lack of significant homology to *E. coli* proteins, considering that proteins having counterparts in many bacterial species, either pathogenic or non-pathogenic have higher probability to have house-keeping functions and therefore are less likely to be good antigens
- Conservation over a panel of at least 5 out of 7 fully sequenced *P. aeruginosa* genomes.
- Useful aminoacid sequence length which is considered to be of at least 150 aa
- Microarray data. *In vitro* expression of *P. aeruginosa* PAO1 derived proteins repertoire was tested to analyse changes in gene expression under anaerobic conditions as those found in the mucus of CF (cystic fibrosis) patients compared with aerobic conditions found in the environment. Priority was assigned to proteins whose expression was maintained in both aerobic and anaerobic cell culture conditions.

[0330] The protein can also adsorb reasonably well to aluminium hydroxide (see also below), which is useful for stable formulation for delivery to humans.

Strain coverage

[0331] In order to evaluate the conservation of the antigens selected, various *P. aeruginosa* clinical isolates were used. *P. aeruginosa* clinical strains were isolated from eight pancreatic-insufficient CF patients attending the CF clinic

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of the Medizinische Hochschule Hannover. *P. aeruginosa* strains from the first positive cultures are designated as "early" isolates, whereas intermediate isolates were collected 1 to 5 years thereafter and late isolates were collected 7 to 16 years after colonization or prior to death or lung transplantation. Strains tested are listed in the following Table.

Table on strain coverage

Strain Genotype	Years of infection
SG1	0
SG57	15,8
SG58	15,8
BT2	0
BT72	15,8
BT73	16,3
AA2	0,5
AA43°	7,5
AA44°	7,5
TR1	0
TR66	12,8
TR67°	13,5
MF1	0
MF51°	10,1
KK1	0
KK71°	12,6
KK72°	12,6
BST2	0,9
BST44	15,8

[0332] The symbol ° indicates the last *P. aeruginosa* strain prior to death or lung transplantation. Genes encoding PSE54, PSE44-4, PSE10-1, PSE21-5, PSE27-1, PSE52-1, PSE53-1, PSE11, PSE41, PSE47-2, were present in all tested strains as confirmed by PCR (polymerase chain reaction).

[0333] Thus, considering the vaccine efficacy in terms of a broader cross-strain protection a vaccine based on any of the best combinations/cocktails as tested in table 2, can be a valid solution in order to extend vaccine coverage against pseudomonas derived infections.

Cloning and expression of P. aeruginosa recombinant proteins

[0334] Cloning and expression of antigens can be performed by standard methods.

[0335] Polypeptides antigens from PA strain PAO1 were PCR-amplified using specific oligonucleotides and PA chromosomal DNA as template. Resulting PCR products were cloned in pET15b (Novagen) using the PIPE method [164], consisting in the PCR amplification of the cloning vector (V-PCR) and in the PCR amplification of the insert (I-PCR). Then, 1 µl of V-PCR and 1 µl of I-PCR are mixed and transformed in chemically competent HK100 cells [165]. I-PCR reactions were set up containing 1 µM each of the forward and reverse primers, 1x Cloned Pfu DNA Polymerase Reaction Buffer, 2.5 units of Pfu Turbo DNA polymerase (Stratagene), 200 µM of each dNTP (Invitrogen) and 50 ng of genomic DNA template. The reactions were conducted as follows: initial denaturation for 2 min at 95 °C, then 25 cycles of 95 °C for 30 s, 55 °C for 45 s, and 68 °C for 3 min followed by a final cool down to 4 °C. V-PCR reactions were identical to the I-PCR reactions but the steps at 68 °C were lasting 14 min and 2 ng of pET15b plasmid were used as DNA template. Correct transformants were selected by PCR screening and DNA plasmid sequencing of the vector-insert junctions. The correct plasmid were then prepared from selected HK100 clones and used to transform BL21(DE3)T1^r cells (Sigma) in order to allow protein expression.

[0336] To express cloned proteins, BL21(DE3)T1^r clones containing pET15b constructs were grown in LB medium containing 100 µg/ml Ampicillin at 37 °C until OD₆₀₀ = 0.5. Protein expression was then induced by adding 1 mM IPTG and growing at the same temperature for additional 3 hrs. Conventional protein extractions and SDS-Page were performed to check protein expression. Western blot techniques known in the art were used to confirm proper expression of tested

P. aeruginosa antigens. Specific antisera from immunized mice were used confirm protein expression. Immunofluorescence techniques known in the art were used to confirm surface localization of tested *P. aeruginosa* antigens using anti-cell wall antibodies as co-localizer and/or a specific anti-antigen serum obtained after mice immunization.

5 **Adjuvant formulation**

[0337] Selected *P. aeruginosa* protein antigen candidates have been formulated with aluminium hydroxide, either individually or as a combination of proteins. The formulations have been optimized for pH and osmolality.

10 [0338] The antigens were formulated as monovalent antigen or multivalent antigens combinations in Aluminium Hydroxide. Each antigen was used at 10 µg/formulation/animal. Aluminium hydroxide was used at 2 mg/ml final concentration, in a 10mM histidine buffer (pH 6.5). Sodium chloride was used to adjust osmolality to physiologic conditions. Formulations were given intratracheal in a final vaccine composition volume of 200 µl/animal.

15 [0339] All monovalent and combination formulations, could be adjusted with respect to a desired pH and osmolality. The formulations had pH in the range 6.2-7.3, and osmolality in the range 248-360 mOsm/kg. Most of the proteins tested, in various monovalent and combination formulations, adsorbed well to the aluminium hydroxide adjuvant.

[0340] The individual PSE54, PSE10-1, PSE21-5, PSE27-1, PSE44-4, PSE52-1, PSE53-1 proteins were completely adsorbed, and could be desorbed without altering their pre-adsorption electrophoretic profile.

20 [0341] Each antigen in a combination of was completely adsorbed, with no inter-antigen competition for the adjuvant. The antigens in a combination of PSE25+PSE54, PSE27-1+PSE44, PSE38-1+PSE11-3, PSE38-1+PSE11-3, PSE41-5+PSE47A-2, PSE41-5+PSE53-1, PSE47A-2+PSE53-1, PSE47A-2+PSE52-1, were also completely adsorbed

[0342] All tested formulations were stable for their pH and osmolality. All antigens remained completely adsorbed to the adjuvant. All antigens maintained their desorption characteristics. There was no evidence of increased degradation or aggregation of antigens after desorption.

25 **Efficacy testing**

[0343] Individual antigens as listed in Table 2 were tested for their ability to protect against intra-tracheal (IT) lethal infection challenge by 5×10^6 cfu of planktonic PAO1 strain. Results are shown in Figure 1.

30 [0344] Recombinant proteins were used to immunize mice for protection studies against *P. aeruginosa*, using as reference strain PAO1. Groups of 10 mice (C57BL/6NCrIBR male 5 weeks old, Charles River Laboratories, Italy) were immunized at day 0, 21 and 35 with different antigens and at day 50 challenged with the homologous *P. aeruginosa* PAO1 referent strain by acute infection. In each boost every mouse received 10 µg or 20 µg of recombinant protein/s adsorbed with alum alone or with 10^7 cfu of heat inactivated PAO1. To obtain antisera mice of all groups were bleeding at day -1, day 34, and day 49. As negative control 10 mice per immunization round were injected with alum alone, while
35 as positive control 10 mice per immunization round were boosted with 10^7 cfu of heat inactivated PAO1 strain. On day 50, mice were infected with 5×10^6 cfu (first lethal dose) of planktonic *P. aeruginosa* PAO1 via intra-tracheal (IT) route. Mice were anesthetized and the trachea directly visualized by a ventral midline incision, exposed and intubated with a sterile, flexible 22-g cannula attached to a 1 ml syringe. A 60 µl inoculum of planktonic bacteria were implanted via the cannula into the lung. Mice were monitored for survival for 120 hrs at intervals of twelve hours and compared with un-
40 vaccinated and PAO1 vaccinated control groups.

[0345] Antigens showed to be able to give an incremental shift in the survival curves compared with the control were listed in table 2, and the best results were seen with PSE21-5, PSE47A-2, PSE52-1, PSE53-1 or PSE54, PSE10, PSE 11-3, PSE 27-1, PSE44-4 and PSE 41-5.

[0346] Further, individual antigens were tested in combination as reported in Table 2.

45 [0347] Table 2 gives a summary of results obtained with various antigens used alone or in combinations *in vivo* in the animal mouse model. Survival data are shown in Table 2. In the statistical significance column, the p value in Mantel-Cox test is calculated against negative control group. Survival curve of each protein was compared with the survival curve of the negative control of the same round in which the protein was tested. Survival was measured for 120 hrs at intervals of twelve hours and compared with un-vaccinated and PAO1 vaccinated control groups. Percentage of mice
50 survival after the 36 hours was evidence of positive immunization results *in vivo*.

[0348] Among the different rounds considering the 30 tested recombinant proteins (Table 2), three proteins (PSE10-1 (PA1178), PSE47A-2 (PA4082), and PSE52-1 (PA4765) had also a highly statistical significance different survival curves when compared with the negative control group (p value in Mantel-Cox test against negative control group 0,0261, 0,0364 and 0,0275 respectively).

55 [0349] On the basis of the analysis of the survival curves of seven additional recombinant proteins it can be predicted that results may also be significantly corroborated by increasing the numbers of animal tested *in vivo* further confirming the preliminary positive and surprising data of PSE11-3 (PA1248), PSE41-5 (PA2407), PSE44-4 (PA3526), PSE53-1 (PA5047), PSE21-5 (PA5112), PSE-54 (PA5340), PSE-27-1 (PA0328).

[0350] In addition when a known antigen, namely OprF-OprI, was used alone to immunize mice in the present animal model a 20% of survival, with a statistical significance of 0,0446 was obtained.

[0351] In order to further improve the survival in this *in vivo* model, specific combinations were also tested by combining together the most promising proteins in order to further increase vaccine efficacy.

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Comparison of Combinations versus its individual polypeptides

[0352] Combinations alias known as cocktails of antigens in a single formulation were also used to immunise mice. The combinations were typically adjuvanted with aluminium hydroxide (see chapter "Adjuvant Formulation") and were administered on days 0, 21 and 35. The immunisations were in C57BL/6NCrIBR male 5 weeks old mice, 10 per group. On day 50 the mice were challenged with a lethal dose of heat inactivated bacteria and survival was then followed for 120 hrs. For comparison, PBS was used as a negative control and PAO1 heat-inactivated as a positive control.

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[0353] The increase in survival, during monitoring for 120 hrs after the immunization schedule and further infection with lethal dose of the *Pseudomonas* homologous strain, when compared to the negative control group, was surprisingly showing best result when the following combinations were tested (Table 2): PSE47A-2+PSE53-1, PSE47A-2+PSE53-1, PSE54+PSE44-4 and PSE54+PSE21-5 being the most promising; whereas PSE47A-2+PSE52-1 combination was less promising.

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[0354] Various tests were performed to compare various combinations to its seven individual polypeptides (i.e PSE54 or PSE21-5 or PSE27-1, PSE44-4, PSE52-1, PSE53-1, PSE47A-2), as well as OprF/I as further positive control or to an antigen-free negative control.

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[0355] Mice were immunized with cocktails of two different proteins. Eight cocktails had statistically different survival curves when compared to the negative control group (considering also the PSE54+OprF-OprI composition).

[0356] In the sixth round, different cocktails of proteins combined with the PSE47A-2 were tested: PSE47A-2+PSE52-1 and PSE47A-2+PSE53-1 were showing a surprising statistical difference respect to the negative control group (p value in Mantel-Cox test against negative control group 0,0374 and 0,0373 respectively).

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[0357] In particular, vaccination with the cocktail PSE47A-2+PSE53-1 resulted surprisingly in 30% of survival, maintain a good statistical significance.

[0358] In the tenth round, different cocktails of proteins combined with the PSE54 were tested. Five cocktails out of eight gave a significantly different mortality curve when compared with negative control group as reported in the Table 2. In particular, vaccination with the cocktails of PSE54+PSE44-4 and PSE54+PSE52-1 antigens gave a very good animal protection resulting in 40% and 33% of animal survival respectively (p value in Mantel-Cox test against negative control group 0,0076 and 0,0142 respectively). When re-tested in the eleventh round, the PSE54+PSE44-4 confirmed the positive result showing an increase of animal survival of 57%. Other cocktails showing better vaccine efficacy when used in combination were: PSE54+PSE21-5, PSE54+PSE53-1 and PSE54+PSE10-1 (p value in Mantel-Cox test against negative control group 0,0332, 0,0085 and 0,0025 respectively).

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[0359] Furthermore, this last cocktail, PSE54+PSE10-1, had comparable results in two different rounds of immunization corroborating the positive and surprising result, resulting in the same survival rate of animals (20%) in both rounds.

[0360] Finally four additional cocktails of different proteins (PSE27-1+PSE44-4, PSE53-1+PSE41-5 and PSE53-1+PSE52-1 and PSE54+PSE27-1) may become even more significant further repeating the experiments in further confirmatory experiments increasing the number of animals.

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[0361] In order to even further improve the capacity of protection and ultimately the vaccine efficacy of selected antigens, combination of three proteins were tested. Seven groups were tested maintaining two fixed proteins PSE54+PSE44-4 plus one variable protein, while others groups tested were with PSE47A-2+PSE52-1+PSE53-1, PSE54+PSE52-1+PSE53-1 and PSE54+PSE53-1+PSE 27-1. Some of these combination did not gave significant animal protection when compared with negative control group whereas when considering e.g. the PSE54+PSE44-4+PSE47A-2 or PSE54+PSE53-1+PSE 27-1 they may provide significant protection simply through confirmatory experiments, obtained by increasing the number of animals (See table 2). Thus, some of the combination of three proteins did not improve protection rather it seemed worse when considering two proteins.

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[0362] However, when considering a further combination adding in the cocktail of antigens also the positive control OprF-OprI fusion was included in the further combinations.

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[0363] When OprF-OprI was used as single fusion protein antigen it showed 20% of survival with a statistical significance of 0.0446, similarly to other single immunization with single promising antigens, whereas when used in combination with PSE54 surprisingly the survival percentage increased to 50% with a similar statistical significance. In addition, the immunization with the following antigens in combination PSE54+PSE27+OprF-OprI showed surprisingly even 60% of survival with a comparable statistical significance, while considering the other combination, namely PSE54+PSE53+OprF-OprI did not show any additive effect or significant immunogenic vaccine efficacy than the single antigens immunization, even in one single immunization using a decrease amount of each single antigen (Table 2). It is reasonable to expect that by increasing the number of animal tested also this specific combination might provide

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significant increase in immunological protection.

[0364] It will be understood that the invention has been described by way of example only and modifications may be made whilst remaining within the scope and spirit of the invention.

TABLE 1: NOMENCLATURE CROSS-REFERENCE

SEQ ID NOs	Locus Tag PAO1 strain	Internal Name	NCBI definitions
1	PA0328	PSE27	outer membrane autotransporter
2	PA1178	PSE10	PhoP/Q low Mg ²⁺ inducible outer membrane protein H1 precursor
3	PA5112	PSE21	esterase EstA
4	PA1248	PSE11	alkaline protease secretion outer membrane protein AprF precursor
5	PA2407	PSE41-5	putative adhesion protein
6	PA3526	PSE44	outer membrane protein precursor
7	PA4082	PSE47	adhesive protein CupB5
8	PA4765	PSE52	Outer membrane lipoprotein Om1A precursor
9	PA5047	PSE53	lipoprotein, putative; peptidase
10	PA5340	PSE54	lipoprotein, putative
11	PA0595	PSE5	OstA precursor
12	PA1954	PSE13	hypothetical protein PA1954
13	PA3692	PSE17	Lipotoxin F
14	PA4370	PSE18	Metalloproteinase outer membrane protein precursor
15	PA4710	PSE19	receptor PhuR precursor
16	PA4735	PSE20	hypothetical protein PA4735
17	PA3647	PSE23	hypothetical protein PA3647
18	PA0126	PSE24	hypothetical protein PA0126
19	PA0189	PSE25	putative porin
20	PA0274	PSE26	hypothetical protein PA0274
21	PA0537	PSE28	putative lipoprotein
22	PA0737	PSE31	putative lipoprotein
23	PA1086	PSE33	flagellar hook-associated FlgK
24	PA1106	PSE34	hypothetical protein PA1106
25	PA1324	PSE36	putative lipoprotein
26	PA1777	PSE38	outer membrane OprF precursor
27	PA2793	PSE42	putative lipoprotein
28	PA3535	PSE45	putative serine protease
29	PA4578	PSE50	hypothetical protein PA4578
30	PA4667	PSE51	TPR domain protein
31	PA4525	PilA	type 4 fimbrial precursor PilA
32	Fusion	OprF/l	Fusion protein
33	PA1092	FliC	Flagellar protein
34	PA1094	FliD	Flagellar protein

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(continued)

SEQ ID NOs	Locus Tag PAO1 strain	Internal Name	NCBI definitions
35	PA1 148	ExoA	Exotoxin A
36	PA0328	PSE27	Fragment without N-terminus
37	PA1178	PSE10	Fragment without N-terminus
38	PA5112	PSE21	Fragment without N-terminus
39	PA1248	PSE11	Fragment without N-terminus
40	PA2407	PSE41-5	Fragment without N-terminus
41	PA3526	PSE44	Fragment without N-terminus
42	PA4082	PSE47-A2	without N-term and translocator domain
43	PA4765	PSE52	Fragment without N-terminus
44	PA5047	PSE53	Fragment without N-terminus
45	PA5340	PSE54	Fragment without N-terminus
46	PA0595	PSE5	Fragment without N-terminus
47	PA1954	PSE13	Fragment without N-terminus
48	PA3692	PSE17	Fragment without N-terminus
49	PA4370	PSE18	Fragment without N-terminus
50	PA4710	PSE19	Fragment without N-terminus
51	PA4735	PSE20	Fragment without N-terminus
52	PA3647	PSE23	Fragment without N-terminus
53	PA0126	PSE24	Fragment without N-terminus
54	PA0189	PSE25	Fragment without N-terminus
55	PA0274	PSE26	Fragment without N-terminus
56	PA0537	PSE28	Fragment without N-terminus
57	PA0737	PSE31	Fragment without N-terminus
58	PA1086	PSE33	Fragment without N-terminus
59	PA1 106	PSE34	Fragment without N-terminus
60	PA1324	PSE36	Fragment without N-terminus
61	PA1777	PSE38	Fragment without N-terminus
62	PA2793	PSE42	Fragment without N-terminus
63	PA3535	PSE45	Fragment without N-terminus
64	PA4578	PSE50	Fragment without N-terminus
65	PA4667	PSE51	Fragment without N-terminus
66	Histidine-Tag	N.A.	N.A.
67	Linker	N.A.	N.A.
68	Linker	N.A.	N.A.
69	Linker	N.A.	N.A.
70	His6	N.A.	Synthetic 6xHis tag

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(continued)

SEQ ID NOs	Locus Tag PAO1 strain	Internal Name	NCBI definitions
71	Glyn	N.A.	Synthetic peptide encompassing 2 to 10 residues, wherein some positions may be absent
72	His _n	N.A.	Synthetic peptide His _n where n = 3, 4, 5, 6, 7, 8, 9, 10 or more
73	(Gly) ₄	N.A.	Synthetic peptide

TABLE 2: MOUSE ANIMAL MODEL RESULTS SUMMARY

Ags	Round	ug Ags	Statistical significance £	Survival %
PSE5	11	10	0.10	0 (0/5)
PSE10	1	10	0.026	0 (0/9)
PSE10-1	8	20	0.56	0 (0/10)
PSE11-3	2	10	0.47*	14 (1/7)
	7	20	0.28*	22 (2/9)
PSE13	4	10	0.55	0 (0/10)
PSE17	11	10	0.35	0 (0/8)
PSE18-2	1	10	0.73	0 (0/8)
PSE19-1	4	10	0.17	0 (0/6)
PSE20	11	10	0.91	12.5 (1/8)
PSE21-5	2	10	0.08*	0 (0/10)
PSE21	11	10	0.19*	50 (5/10)
PSE23-1	1	10	0.61	0 (0/9)
PSE24-1	1	10	0.19	0 (0/8)
PSE25-1	4	10	0.10	0 (0/10)
	8	20	0.90	0 (0/10)
PSE26	3	10	0.32	0 (0/9)
PSE27-1	2	10	0.91	0 (0/10)
	4	10	0.21*	0 (0/10)
	7	20	0.80	11 (1/9)
PSE28-2	2	10	0.37	0 (0/10)
PSE31-2	2	10	1	0 (0/10)
	11	10	0.76	10 (1/10)
PSE33	11	10	0.61	0 (0/9)
PSE34	1	10	0.17	0 (0/9)
PSE36-3	1	10	1	0 (0/10)
PSE38-1	2	10	0.53	22 (2/9)
PSE41-5	1	10	0.34*	0 (0/10)
	6	20	0.25	0 (0/9)
	7	20	0.65*	0 (0/10)
PSE42-1	4	10	0.55	13 (1/8)
PSE44-4	2	10	0.08*	0 (0/9)
	7	20	0.28*	22 (2/9)
PSE45-2	4	10	0.32	0 (0/8)
PSE47-3	4	10	0.06	0 (0/5)
PSE47A-2	2	10	0.0364	10 (1/10)
	4	10	0.55	0 (0/10)
	6	20	0.26	20 (2/10)

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(continued)

	Ags	Round	ug Ags	Statistical significance £	Survival %
		9	20	0.27	20 (2/10)
5	PSE50	3	10	0.96	0 (0/9)
	PSE51	3	10	1	0 (0/8)
	PSE52	3	10	0.0275	0 (0/9)
	PSE52-1	6	20	0.0208	10 (1/10)
	PSE53	3	10	0.07*	0 (0/9)
10	PSE53-1	6	20	0.22*	0 (0/8)
		7	20	0.25*	22 (2/9)
	PSE54	3	10	0.17*	10 (1/10)
		8	20	0.88	0 (0/10)
15		9	20	0.16*	0 (0/8)
		14	10	0.19*	60 (6/10)
	PSE25+PSE54	8	10+10	0.49	0 (0/10)
	PSE27-1+PSE44	7	10+10	0.38*	0 (0/10)
	PSE38-1+PSE11-3	9	10+10	0.004#	0 (0/9)
20	PSE41-5+PSE52-1	6	10+10	0.27	11 (1/9)
	PSE41-5+PSE47A-2	6	10+10	0.98	0 (0/4)
	PSE41-5+PSE53-1	7	10+10	0.55*	10 (1/10)
	PSE47A-2+PSE53-1	6	10+10	0.0373	30 (3/10)
25	PSE47A-2+PSE53-1	9	10+10	0.09	0 (0/10)
	PSE47A-2+PSE52-1	6	10+10	0.0374	0 (0/7)
	PSE47A-2+PSE52-1	9	10+10	0.06	0 (0/9)
	PAE47A-2+PSE21-5	9	10+10	0.28	11 (1/9)
	PSE47A-2+PSE44-4	9	10+10	0.34	0 (0/9)
30	PSE47A-2+PSE38-1	9	10+10	0.003#	0 (0/10)
	PSE47A-2+PSE11-3	9	10+10	0.01#	0 (0/10)
	PSE53-1+PSE52-1	6	10+10	0.20*	0 (0/9)
	PSE54+PSE10-1	8	10+10	0.0154	20 (2/10)
35		10	10+10	0.0025	20 (2/10)
	PSE54+PSE47A-2	10	10+10	0.55	10 (1/10)
	PSE54+PSE11-3	10	10+10	0.31	10 (1/10)
	PSE54+PSE52-1	10	10+10	0.0142	33 (3/9)
		11	10+10	0.96	0 (0/3)
40	PSE54+PSE53-1	10	10+10	0.0085	12.5 (1/8)
	PSE54+ PSE53	13	10+10	0.61	22 (2/9)
	PSE54+PSE21-5	7	10+10	0.0332	14 (1/7)
	PSE54+PSE21	13	10+10	0.0213	40 (4/10)
45		14	10+10	0.13*	70 (7/10)
	PSE54+PSE27-1	10	10+10	0.20*	22 (2/9)
	PSE54+ PSE27	13	10+10	0.16*	10 (1/10)
		14	10+10	0.052*	80 (8/10)
	PSE54+PSE44-4	10	10+10	0.0076	40 (4/10)
50		11	10+10	0.14*	57.1 (4/7)
	PSE54+OprF-OprI	13	10+10	0.0403	50 (5/10)
	PSE10-1+PSE25-1	8	10+10	0.44	0 (0/7)
	PSE47A-2+PSE52-1+PSE53-1	9	10+10+10	0.06	0 (0/8)
55	PSE54+PSE44-4+PSE10-1	12	10+10+10	0.69	0 (0/10)
	PSE54+PSE44-4+PSE21-5	12	10+10+10	0.34	0 (0/10)
	PSE54+PSE44-4+PSE27	12	10+10+10	0.32	0 (0/10)
	PSE54+PSE44-4+PSE52	12	10+10+10	0.61	0 (0/5)

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(continued)

Ags	Round	ug Ags	Statistical significance £	Survival %
PSE54+PSE44-4+PSE53-1	12	10+10+10	0.25	0 (0/7)
5 PSE54+PSE44-4+ PSE47A-2	12	10+10+10	0.17*	16.6 (1/6)
PSE54+PSE44-4+PSE11	12	10+10+10	0.46	0 (0/10)
PSE54+PSE52-1+PSE53-1	12	10+10+10	0.68	0 (0/4)
PSE54+PSE27+OprF-OprI	13	10+10+10	0.0021	60 (6/10)
10 PSE54+ PSE53+OprF-OprI	13	10+10+10	0.17*	20 (2/10)
PSE54+PSE53+ PSE27	13	10+10+10	0.08*	20 (2/10)
PSE54+PSE53+ PSE27	13	6.7+6.7+6.7	0.17*	20 (2/10)
OprF-OprI	11	10	0.28	0 (0/8)
	12	10	0.43	10 (1/10)
15	13	10	0.0446	20 (2/10)

Legend of table 2:

p value in Mantel-Cox test against negative control group: Survival curve of each protein was compared with the survival curve of the negative control of the same round in which the protein was tested. Survival was measured for 120 hrs at intervals of twelve hours and compared with un-vaccinated and PAO1 vaccinated control groups. Percentage of mice survival after the 36 hours was evidence of positive immunization results *in vivo*.

* t-test significant with increased animal number: antigen vs negative control.

t-test significant: antigen vs. negative control significant but mice immunized with the antigens dead before the negative controls. Nd: not done

[0365] Further embodiments of the present invention are listed below:

1. An immunogenic composition comprising one or more antigens selected from the list of: a PSE54 (PA5340) antigen; a PSE44-4 (PA3526) antigen; a PSE10-1 (PA1178) antigen; a PSE21-5 (PA5112) antigen; a PSE27-1 (PA0328) antigen; a PSE52-1 (PA4765) antigen; a PSE53-1 (PA5047) antigen; PSE11-3 (PA1248) antigen; a PSE41-5 (PA2407) antigen; a PSE47A-2 (PA4082); PSE5-1 (PA0595); PSE13-2 (PA1954); PSE17-1 (PA3692); PSE18-2 (PA4370); PSE20-1 (PA4735); PSE23-1 (PA3647); PSE24-1 (PA0126); PSE25-1 (PA0189); PSE26-1 (PA0274); PSE28-2 (PA0537); PSE31-2 (PA0737); PSE33-2 (PA1086); PSE42-1 (PA2793); PSE45-2 (PA3535); PSE50-1 (PA4578); PSE51-4 (PA4667); PSE19-1 (PA4710); PSE34-1 (PA1106); PSE36-3 (PA1324); PSE38-1 (PA1777).

2. An immunogenic composition according to embodiment 1 wherein antigens are selected from any of: a PSE54 (PA5340) antigen; a PSE44-4 (PA3526) antigen; a PSE21-5 (PA5112) antigen; a PSE27-1 (PA0328) antigen; a PSE53-1 (PA5047) antigen; a PSE41-5 (PA2407) antigen; a PSE47A-2 (PA4082); PSE5-1 (PA0595); PSE13-2 (PA1954); PSE17-1 (PA3692); PSE18-2 (PA4370); PSE20-1 (PA4735); PSE23-1 (PA3647); PSE24-1 (PA0126); PSE25-1 (PA0189); PSE26-1 (PA0274); PSE28-2 (PA0537); PSE31-2 (PA0737); PSE33-2 (PA1086); PSE42-1 (PA2793); PSE45-2 (PA3535); PSE50-1 (PA4578); PSE51-4 (PA4667); PSE34-1 (PA1106); PSE36-3 (PA1324).

3. The composition of embodiment 1, wherein the one or more antigen is selected from: a PSE 54 (PA5340) antigen, PSE21-5 (PA5112) antigen; a PSE27-1 (PA0328) antigen; PSE41-5 (PA2407); a PSE44-4 (PA3526) antigen; a PSE47A-2 (PA4082) antigen; a PSE53-1 (PA5047) antigen, or a PSE52-1 (PA4765) antigen; a PSE10-1 (PA1178) antigen; a PSE11-3 (PA1248).

4. The composition of embodiment 1, comprising at least two antigens in combination selected from the list: a PSE54 (PA5340) antigen; a PSE44-4 (PA3526) antigen; a PSE10-1 (PA1178) antigen; a PSE21-5 (PA5112) antigen; a PSE27-1 (PA0328) antigen; a PSE52-1 (PA4765) antigen; a PSE53-1 (PA5047) antigen; PSE11-3 (PA1248) antigen; a PSE41 (PA2407) antigen; a PSE47A-2 (PA4082); PSE5-1 (PA0595); PSE13-2 (PA1954); PSE17-1 (PA3692); PSE18-2 (PA4370); PSE20-1 (PA4735); PSE23-1 (PA3647); PSE24-1 (PA0126); PSE25-1 (PA0189); PSE26-1 (PA0274); PSE28-2 (PA0537); PSE31-2 (PA0737); PSE33-2 (PA1086); PSE42-1 (PA2793); PSE45-2 (PA3535); PSE50-1 (PA4578); PSE51-4 (PA4667); PSE19-1 (PA4710); PSE34-1 (PA1106); PSE36-3 (PA1324); PSE38-1 (PA1777).

5. The composition according to embodiment 4, further comprising any other antigens selected from the list: PilA,

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OprF-OprI, FliC, FliD, ExoA, and wherein one of the antigen is PSE 54.

6. The composition of embodiment 4, comprising at least one antigen selected from: PSE10-1 (PA1178), PSE52-1 (PA4765), PSE53-1 (PA5047), PSE21-5 (PA4765) and wherein the other antigen in PSE54 (PA5340).

7. The composition of embodiment 4, comprising two or more antigens selected from the group consisting of: a PSE54 (PA5340) antigen; a PSE10-1 (PA1178) antigen; a PSE44-4 (PA3526) antigen; a PSE52-1 (PA4765) antigen; a PSE53-1 (PA5047) antigen; a PSE21-5 (PA5112) antigen; a PSE27-1 (PA0328) antigen; a PSE47A-2 (PA4082) antigen or OprF-OprI.

8. The composition of any preceding embodiment, wherein one or more of said antigens is adsorbed to an aluminium hydroxide adjuvant, and optionally wherein the composition includes a histidine buffer.

9. The composition of any preceding embodiment, further comprising: one or more conjugates of (i) a *P. aeruginosa* exopolysaccharide and (ii) a carrier protein.

10. An immunogenic composition comprising the polypeptide of any preceding embodiments, and further comprising one or more of:

(A) one or more conjugates of (i) a *S. aureus* exopolysaccharide;

(B) one or more protein antigens of (i) a *S. aureus* or

(C) one or more pathogenic *E. coli* antigen/s

(D) one or more pathogenic *B. cenocepacia* antigen/s

11. An immunogenic composition comprising the polypeptide of any of embodiment 1 or 2 and one or more of (i) a OprF-OprI antigen; (ii) a FliC antigen; (iii) a FliD antigen and/or (iv) a PilA antigen.

12. The composition of any preceding embodiments, including an adjuvant.

13. A polypeptide comprising amino acid sequence having 80% or more identity to an amino acid sequence selected from anyone of SEQ ID NOs: 1-35 or SEQ ID NOs: 36-65

14. A pharmaceutical composition comprising the polypeptide of any one of embodiments 11-12 or 13.

15. Immunogenic composition of any one of any preceding embodiments, for use in raising an immune response in a mammal.

16. Immunogenic composition of any one of any preceding embodiments, for use as prophylactic or therapeutic vaccine against nosocomial infections.

17. A method for raising an immune response in a mammal comprising the step of administering to the mammal an effective amount of the polypeptide or composition of any preceding embodiment.

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45 Asp Tyr Arg Met Asn Ser Tyr Met Ala Ser Ala Phe Val Gln Tyr Gln
 435 440 445

Glu Asn Arg Trp Trp Ala Asp Ala Ala Leu Thr Gly Gly Tyr Leu Asp
 450 455 460

50 Tyr Asp Asp Leu Lys Arg Lys Phe Ala Leu Gly Gly Gly Glu Arg Ser
 465 470 475 480

Glu Lys Gly Asp Thr Asn Gly His Leu Trp Ala Phe Ser Ala Arg Leu
 485 490 495

55 Gly Tyr Asp Ile Ala Gln Gln Ala Asp Ser Pro Trp His Leu Ser Pro

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Gln Thr Thr Thr Arg Gly Asp Phe Lys Glu Asp Arg Asp Tyr Asp Ser
85 90 95

5 Tyr Val Ser Thr Leu Ser Leu Gln Gln Pro Leu Phe Asp Tyr Glu Ala
100 105 110

10 Phe Ser Arg Tyr Arg Lys Gly Val Ala Gln Ala Leu Leu Ser Asp Glu
115 120 125

15 Arg Phe Arg Ser Gln Ser Gln Glu Leu Leu Val Arg Val Leu Glu Ala
130 135 140

Tyr Thr Gly Ala Leu Leu Ala Gln Asp Gln Ile Glu Leu Ala Arg Ala
145 150 155 160

20 Gln Lys Arg Ser Tyr Arg Glu Gln Phe Gln Leu Asn Gln Arg Gln Phe
165 170 175

25 Glu Arg Gly Asn Gly Thr Arg Thr Asp Thr Leu Glu Thr Gln Ala Arg
180 185 190

Phe Asn Leu Ala Gln Ala Gln Glu Ile Glu Ala Arg Asp Ser Gln Asp
195 200 205

30 Ala Ala Leu Arg Glu Leu Glu Arg Leu Val Gly Ala Pro Leu Glu Ile
210 215 220

35 Ala Asp Leu Ala Pro Leu Gly Glu Arg Phe Gln Val Arg Pro Leu Ser
225 230 235 240

40 Pro Ala Ser Tyr Thr Ala Trp Arg Asp Leu Ala Leu Ala Glu Asn Pro
245 250 255

Glu Leu Ala Ser Leu Arg His Ala Val Asp Val Ala Arg Tyr Glu Val
260 265 270

45 Glu Gln Asn Arg Ala Asp Phe Leu Pro Arg Leu Gly Leu Tyr Ala Ser
275 280 285

50 Thr Gly Lys Ser Lys Ser Gly Ser Glu Asn Thr Tyr Asn Gln Arg Tyr
290 295 300

Glu Thr Asp Ser Val Gly Ile Gln Leu Ser Val Pro Leu Phe Ser Gly
305 310 315 320

55 Gly Glu Thr Leu Ala Ala Thr Arg Gln Ala Thr His Arg Met Glu Lys

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Glu Val Val Pro Leu Ile Pro Ala Gly Phe Asn Pro His Ala Tyr Glu
 65 70 75 80
 5 Pro Arg Ala Glu Asp Ile Lys Arg Ile Gly Thr Leu Asp Val Val Val
 85 90 95
 10 Leu Asn Gly Val Gly His Asp Asp Phe Ala Glu Arg Met Ile Ala Ser
 100 105 110
 15 Ser Glu Lys Pro Gly Ile Pro Val Ile Glu Ala Asn Ala Lys Val Pro
 115 120 125
 20 Leu Leu Ala Ala Thr Gly Met Ala Ala Arg Gly Ala Gly Lys Val Val
 130 135 140
 25 Asn Pro His Thr Phe Leu Ser Ile Ser Ala Ser Ile Thr Gln Val Asn
 145 150 155 160
 30 Thr Ile Ala Arg Glu Leu Gly Lys Leu Asp Pro Ala Asn Ala Lys Ala
 165 170 175
 35 Tyr Thr Arg Asn Ala Arg Ala Tyr Ala Lys Arg Leu Arg Ala Leu Arg
 180 185 190
 40 Ala Asp Ala Leu Ala Arg Leu Asn Lys Ala Pro Ala Ala Asp Phe Arg
 195 200 205
 45 Val Ala Thr Ile His Gly Ala Tyr Asp Tyr Leu Leu Arg Glu Phe Gly
 210 215 220
 50 Leu Glu Val Thr Ala Val Val Glu Pro Ala His Gly Ile Glu Pro Ser
 225 230 235 240
 55 Pro Ser Gln Leu Lys Lys Thr Ile Asp Gln Leu Lys Ala Leu Asp Val
 245 250 255
 60 Lys Val Ile Phe Ser Glu Ile Asp Phe Pro Ser Thr Tyr Val Glu Thr
 260 265 270
 65 Ile Gln Arg Glu Ser Gly Val Lys Leu Tyr Ser Leu Ser His Ile Ser
 275 280 285
 70 Tyr Gly Asp Tyr Ser Ala Gly Lys Tyr Glu Glu Glu Met Ala Arg Asn
 290 295 300
 75 Leu Asp Thr Val Val Arg Ala Ile Gln Glu Ser Gly Ala

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Arg Asp Leu Ser Arg Arg Arg Ala Leu Ala Val Gln Glu Tyr Leu Lys
 225 230 235 240
 5 Ser Asn Gly Val Pro Glu Ser Gln Ile Asn Val Arg Phe Tyr Gly Glu
 245 250 255
 10 Arg Tyr Pro Leu Val Ala Asn Asn Ser Ala Ala Asn Arg Ala Arg Asn
 260 265 270
 15 Arg Arg Val Thr Val His Leu Ser Arg Glu Ala Val Val Glu Pro Ala
 275 280 285
 20 Thr Glu Ala Pro Lys Ala Glu Asp Lys Pro Ala Pro Pro Ala Ala Glu
 290 295 300
 25 Pro Ala Ala Pro Lys Pro Pro Ala Ala Ser Leu Gln Gly Lys Pro Thr
 305 310 315 320
 30 Val
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 <211> 1018
 <212> PRT
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 40 Lys Ala Ala Ile Ala Ser Val Leu Ala Leu Leu Gly Ala Thr Ala Leu
 35 40 45
 45 Ala Pro Ala Tyr Ala Leu Pro Ser Gly Gly Thr Val Val Gly Gly Ser
 50 55 60
 50 Ala Asn Gly Glu Ile His Leu Ser Gly Gly Asn Ser Leu Ser Val Asn
 65 70 75 80
 55 Gln Lys Val Asp Lys Leu Ile Ala Asn Trp Asp Ser Phe Ser Val Ala
 85 90 95
 Ala Gly Glu Arg Val Ile Phe Asn Gln Pro Ser Ser Ser Ser Ile Ala
 100 105 110

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Leu Asn Arg Val Ile Gly Thr Lys Ala Ser Asp Ile Gln Gly Arg Ile
 115 120 125
 5 Asp Ala Asn Gly Gln Val Phe Leu Val Asn Pro Asn Gly Val Leu Phe
 130 135 140
 Gly Arg Gly Ala Gln Val Asn Val Gly Gly Leu Val Ala Ser Thr Leu
 10 145 150 155 160
 Asp Ile Thr Asp Ala Glu Phe Asn Gly Asn Ser Ser Arg Tyr Arg Phe
 15 165 170 175
 Thr Gly Pro Ser Thr Asn Gly Val Leu Asn His Gly Gly Ala Ile Thr
 180 185 190
 20 Ala Ala Glu Gly Gly Ser Ile Ala Leu Leu Gly Ala Gln Val Asp Asn
 195 200 205
 Arg Gly Thr Val Leu Ala Gln Met Gly Gly Val Gly Leu Gly Ala Gly
 25 210 215 220
 Ser Asp Leu Thr Leu Asn Phe Asp Gly Asn Lys Leu Leu Asp Ile Arg
 225 230 235 240
 30 Val Asp Ala Gly Val Ala Asn Ala Leu Ala Ser Asn Gly Gly Leu Leu
 245 250 255
 Lys Ala Asp Gly Gly Arg Val Leu Met Ala Ala Arg Thr Ala Asn Ala
 35 260 265 270
 Leu Leu Asn Thr Val Val Asn Ser Gln Gly Ala Ile Glu Ala Arg Ser
 275 280 285
 40 Leu Arg Gly Lys Asn Gly Arg Ile Val Leu Asp Gly Gly Pro Asp Gly
 290 295 300
 Lys Val Met Val Gly Gly Ala Leu Ser Ala Asn Ala Leu Asn Gly Pro
 45 305 310 315 320
 Gly His Gly Gly Thr Val Glu Val Arg Gly Gln Ala Val Glu Val Ala
 50 325 330 335
 Leu Gly Thr Gln Val Asn Thr Leu Ala Ser Asn Gly Leu Asn Gly Thr
 340 345 350
 55 Trp Lys Ile Ala Ala Asp Lys Ile Asp Val Arg Pro Ser Ala Val Ser
 355 360 365

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Asp Gly Val Thr Val His Ala Asp Thr Leu Ser Arg Asn Leu Ala Ser
 370 375 380
 5 Thr Asn Ile Glu Leu Val Ser Thr Lys Gly Asp Leu Asp Leu Asp Gly
 385 390 395 400
 10 Ser Val Asn Trp Ala Ser Gly Asn Arg Leu Gly Leu Gly Ser Ala Ala
 405 410 415
 15 Asp Leu Thr Leu Asn Gly Arg Leu Asn Ala Ser Gly Ala Lys Ala Gly
 420 425 430
 20 Leu Glu Leu Lys Ala Glu Gly Ala Ile Asp Ile Asn Asp Lys Ile Val
 435 440 445
 25 Arg Val Asn Gly Thr Ala Ser Val Ser Leu Ala Gly Ala Asn Ala Thr
 465 470 475 480
 30 Tyr Val Ser Gly Gly Tyr Tyr Tyr Thr Val Val Gln Asn Leu Ala Gln
 485 490 495
 35 Leu Gln Ala Ile Asn Lys Asn Leu Asp Gly Leu Tyr Val Leu Gly Gly
 500 505 510
 40 Asn Ile Leu Gly Gly Ser Tyr Tyr Cys Thr Ala Leu Gln Ser Ile Gly
 515 520 525
 45 Gly Pro Ala Gly Val Phe Ser Gly Thr Leu Asp Gly Leu Gly Asn Ser
 530 535 540
 50 Ile Gly Asn Leu Ser Ile Ser Asn Thr Gly Pro Asn Val Gly Leu Phe
 545 550 555 560
 55 Ala Arg Ser Ser Gly Thr Leu Ser Asn Leu Lys Leu Asn Asn Leu Arg
 565 570 575
 Val Ser Asp Asn Thr Tyr Gly Ser Gly Pro Ser Ser Leu Gly Ala Leu
 580 585 590
 Val Gly Ile Asn Ser Gly Arg Ile Ala Asn Val Ser Ala Ser Gly Val
 595 600 605
 Ser Val Val Gly Ser Arg Leu Arg Ser Asn Ala Leu Gly Gly Leu Val

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	610					615						620				
5	Gly 625	Arg	Asn	Ile	Ser	Gly 630	Gln	Ile	Ala	Asn	Ala 635	Ser	Val	Ser	Gly	Gly 640
10	Val	Thr	Gly	Tyr	Ala 645	Ala	Ser	Thr	Ala	Val 650	Gly	Gly	Leu	Val	Gly 655	Glu
15	Asn	Phe	Thr	Thr 660	Ala	Trp	Gly	Pro	Glu 665	Ala	Val	Ile	Glu	Asn 670	Ala	His
20	Ser	Asn	Val 675	His	Val	Ala	Ala	Gln 680	Ser	Thr	Glu	Arg	Asn 685	Ser	Leu	Gly
25	Gly	Val 690	Gly	Gly	Leu	Val	Gly 695	Leu	Asn	Ala	Lys	Gly 700	Met	Ile	Arg	Ala
30	Ser 705	Gly	Ser	Gln	Gly	Lys 710	Val	Glu	Thr	Tyr 715	Arg	Pro	Gly	Leu	Asn	Val 720
35	Gly	Gly	Leu	Val	Gly 725	Tyr	Asn	Met	Phe	Gly 730	His	Val	Ser	Asp	Ser	Ser 735
40	Ala	Ser	Gly	Gln 740	Val	Glu	Ala	Gly	Gly 745	Ala	Gly	Asn	Thr	Gly	Gly	Leu
45	Val	Gly	Leu 755	Ser	Ser	Gly	Gly	Glu 760	Ile	Phe	Arg	Ser	Gln 765	Ala	Ser	Gly
50	Ser 770	Val	Tyr	Ser	Lys	Gly	Gly 775	Leu	Ala	Thr	Gly	Gly 780	Leu	Ile	Gly	Lys
55	Ala 785	Glu	Gly	Asn	Gly	Met 790	Leu	Gly	Asn	Leu	Lys 795	Ala	Ser	Gly	Ser	Val 800
60	Thr	Asp	Gln	Gly 805	Gly	Ala	Asp	Leu	Gly	Gly 810	Leu	Val	Gly	Asn 815	Asn	Ser
65	Gln	Ser	Ala	Ile 820	Glu	Thr	Ala	Glu	Ala 825	Thr	Gly	Lys	Val	Ser 830	Gly	Gly
70	Ser	Asn	Ser 835	Arg	Val	Gly	Gly	Leu 840	Ile	Gly	His	Asn 845	Leu	Gly	Gly	Ser
75	Val 850	Ala	His	Ala	Ile	Ser	Arg 855	Gly	Asp	Val	Ser	Gly 860	Gly	Phe	Asn	Ser

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Leu Val Gly Gly Leu Val Gly His Asn Gly Gly Glu Leu Val Asn Val
 865 870 875 880
 5 Asp Ala Ser Gly Arg Val Ser Ala Ala Ala Ser Ala Ser Val Gly Gly
 885 890 895
 Leu Val Gly Ser Asn Ala Gly Ser Ile Leu Ser Ala Arg Ser Ser Ser
 900 905 910
 10 Thr Val Asn Gly Ser Gly Arg Ser Arg Ile Gly Gly Leu Val Gly Glu
 915 920 925
 15 Asn Gln Ile Gln Gly Arg Ile Val Ser Ser Met Ser Glu Gly Thr Val
 930 935 940
 Ser Gly Asp Tyr Tyr Val Ser Met Gly Gly Leu Ala Gly Leu Asn Leu
 945 950 955 960
 20 Gly Ser Ile Glu Tyr Ser Gly Val Ser Gly Lys Ile Asp Phe Lys Pro
 965 970 975
 25 Gln Ser His Tyr Gly Gln Ile Tyr Gly Ala Gln Val Gly Glu Asn His
 980 985 990
 Gly Val Leu Gly Gly Asn Tyr Val Ile Gly Glu Ala Ala Leu Leu Pro
 995 1000 1005
 30 Pro Ala Gly Ile Asp Tyr Gly Asn Ile Trp
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 <211> 176
 <212> PRT
 <213> Pseudomonas aeruginosa
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 45 Ala Ala Leu Ala Gly Cys Ser Phe Pro Gly Val Tyr Lys Ile Asp Ile
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 Gln Gln Gly Asn Val Val Thr Gln Asp Met Ile Asp Gln Leu Arg Pro
 35 40 45
 50 Gly Met Thr Arg Arg Gln Val Arg Phe Ile Met Gly Asn Pro Leu Ile
 50 55 60
 55 Val Asp Thr Phe His Ala Asn Arg Trp Asp Tyr Leu Tyr Ser Ile Gln

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His Val Thr Ala Arg His Ser Val Arg Gln Gln Ser Gln Ala Ser Ala
 130 135 140

5
 Trp Asn Ile Leu Gly Gln Ala Val Ala Ile Gly Thr Gly Val Gly Ala
 145 150 155 160

10
 Ala Gly Asp Leu Ala Asn Val Leu Gly Thr Ala Phe Val Arg Gly Tyr
 165 170 175

15
 Gly Arg Asp Met Glu Leu Glu Ala Asp Gly Leu Gly Ala Gln Tyr Leu
 180 185 190

20
 Ala Arg Ala Gly Tyr Asp Pro Thr Ala Met Ile Gln Val Val Arg Val
 195 200 205

25
 Leu Lys Asn Gln Glu Asp Phe Ala Arg Glu Glu Ala Ala Arg Asn Gly
 210 215 220

30
 Gln Ala Val Gln Ala Gly Gly Tyr His Gly Leu Phe Asp Thr His Pro
 225 230 235 240

35
 Asp Asn Asp Arg Arg Leu Gln Glu Val Val Gly Pro Ala Arg Gln Leu
 245 250 255

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 Ala Asn Gly Gln Gln Glu Val Gly Arg Glu Val Phe Leu Arg His Leu
 260 265 270

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 Glu Gly Met Pro Phe Gly Asp Ser Ala Ser Ala Gly Val Arg Arg Gly
 275 280 285

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 Gln Asn Phe Tyr His Ala Glu Leu Asp Phe Thr Leu Ser Tyr Pro Ala
 290 295 300

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 Gly Trp Lys Ile Leu Asn Gln Pro Ser Ala Leu Leu Gly Tyr Pro Ala
 305 310 315 320

60
 Asp Glu Gln Ser Phe Ile Gly Met Lys Leu Val Pro His Asp Ser Arg
 325 330 335

65
 Leu Thr Pro Ala Glu Phe Leu Arg Lys Asn Ala Gly Gln Arg Leu Ala
 340 345 350

70
 Gln Glu Glu Ser Leu Lys Gln Ala Gly Leu Asn Gly Tyr Thr Ala Val
 355 360 365

75
 Val Pro Gly Asn Pro Ala Arg Arg Val Ala Val Ile Tyr Gln Gly Asp

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370 375 380

5 Arg Ala Tyr Leu Phe Val Gly Val Val Lys Val Gly Ser Leu Glu Thr
385 390 395 400

10 Gln Asp Asp Arg Phe Leu Ser Val Ile Arg Ser Phe Arg Pro Leu Arg
405 410 415

15 Asp Lys Glu Arg Ala Leu Ala Gln Pro Arg Arg Leu His Leu Val Gln
420 425 430

20 Val Lys Ala Gly Gln Thr Leu Glu Gln Leu Ala Ala Gly Gly Glu Gly
435 440 445

25 Ser Leu Ser Asp Ser Val Ala Arg Leu Arg Leu Leu Asn Asp Leu Tyr
450 455 460

30 Pro Ser Gly Glu Pro Arg Pro Gly Asp Trp Leu Lys Val Val Arg
465 470 475

35 <210> 10
<211> 243
<212> PRT
<213> Pseudomonas aeruginosa

40 Met Arg Arg Val Ile Phe Leu Ala Ala Ala Thr Leu Leu Ala Gly
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45 Cys Ala Gly Thr Ala Asp Pro Ser Gly Thr Trp Ile Asn Gln Ala Ala
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50 Ile Asp Ala Ala Ser Lys Asp Gly Lys Leu Arg Glu Ala Leu Leu Ala
35 40 45

55 Tyr Gly Pro Asn Leu Glu Trp Lys Leu Asp Ser Lys Ala Gly Glu Ala
50 55 60

60 Thr Phe Ser Asn Gly Phe Glu Leu Gly Glu Gly Thr Leu Ser Lys Ser
65 70 75 80

65 Asp Asp Glu His Trp Lys Val Ala Phe Tyr Gly Asp Asp Asn Gln Glu
85 90 95

70 Ser Leu Glu Leu Asp Gly Lys Glu Leu Ile Gln Gln Ala Ser Ala Asn
100 105 110

75 Gly Pro Glu Gln Arg Phe Arg Arg Leu Asp Pro Gln Pro Ala Ala Ser
115 120 125

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Ser Pro Ala Gly Ser Gly Phe Glu Arg Ala Leu Tyr Gly Ser Tyr Leu
 130 135 140
 5 Lys Gly Ser Trp Lys Ile Arg Glu Gly Gln Gly Gln Gly Gly Lys Val
 145 150 155 160
 10 Glu Phe Gln Ala Asn Gly Leu Val Ser Gly Leu Pro Gly Ala Glu Arg
 165 170 175
 Tyr Ala Leu Cys Leu Ala Gly Asp Cys Ala Ala Met Ser Gly Asp Asn
 180 185 190
 15 Asp Ser Ile Trp Leu Gln Gln Gly Asn Arg Gly Arg Glu Leu Leu Phe
 195 200 205
 20 Ser Leu Asp Asp Asp Glu Leu Gln Leu Phe Glu Ala Val Asn Thr Ala
 210 215 220
 25 Gly Ala Asn Glu Met Pro Ser Tyr Val Pro Gly Lys Arg Val Trp Leu
 225 230 235 240
 Leu Glu Arg
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 <210> 11
 <211> 924
 <212> PRT
 <213> Pseudomonas aeruginosa
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 40 Thr Gly Ser Leu Leu Ala Leu Gln Pro Val Ala Ala Leu Thr Val Gln
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 45 Ala Ala Asp Gln Phe Asp Cys Lys Val Ser Ala Thr Gly Gly Trp Asp
 35 40 45
 50 Cys Ser Pro Leu Gln Asn Ala Asn Ala Asn Leu Pro Pro Arg Pro Ala
 50 55 60
 55 His Thr Ala Thr Ser Val Ser Thr Ala Ala Ala Gly Ser Ser Val Ser
 65 70 75 80
 Gly Ser Gly Gly Glu Thr Val Glu Ala Glu Pro Thr Gln Arg Leu Val
 85 90 95

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Thr Glu Ser Gly Gly Arg Ala Leu Lys Ser Arg Ser Ala Asp Tyr Ser
 100 105 110

5 His Leu Asp Trp Ile Pro Arg Glu Lys Leu Thr Ala Ala Gln Leu Ala
 115 120 125

10 Glu Ile Gly Pro Tyr Cys Gly Gly Ser Tyr Ile Glu Pro Val Arg Pro
 130 135 140

15 Gly Met Asp Asp Gly Ala Pro Ser Asp Glu Ser Pro Thr Tyr Val Ser
 145 150 155 160

Ala Lys Ala Ser Arg Tyr Glu Gln Glu Lys Gln Ile Ala Thr Leu Ala
 165 170 175

20 Gly Asp Val Val Leu Arg Gln Gly Ser Met Gln Val Glu Gly Asp Glu
 180 185 190

25 Ala Asn Leu His Gln Leu Glu Asn Arg Gly Glu Leu Val Gly Asn Val
 195 200 205

Lys Leu Arg Asp Lys Gly Met Leu Val Val Gly Asp His Ala Gln Val
 210 215 220

30 Gln Leu Asp Asn Gly Glu Ala Gln Val Asp Asn Ala Glu Tyr Val Ile
 225 230 235 240

35 His Lys Ala His Ala Arg Gly Ser Ala Leu Tyr Ala Lys Arg Ser Glu
 245 250 255

40 Asn Ala Ile Ile Met Leu Lys Asp Gly Thr Tyr Thr Arg Cys Glu Pro
 260 265 270

Ser Ser Asn Ala Trp Thr Leu Lys Gly Asn Asn Val Lys Leu Asn Pro
 275 280 285

45 Ala Thr Gly Phe Gly Thr Ala Thr Asn Ala Thr Leu Arg Val Lys Asp
 290 295 300

50 Phe Pro Val Phe Tyr Thr Pro Tyr Ile Tyr Phe Pro Ile Asp Asp Arg
 305 310 315 320

Arg Gln Ser Gly Phe Leu Pro Pro Ser Phe Ser Ser Thr Ser Asp Thr
 325 330 335

55 Gly Phe Thr Leu Val Thr Pro Tyr Tyr Phe Asn Leu Ala Pro Asn Tyr
 340 345 350

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Asp Ala Thr Leu Tyr Pro Arg Tyr Met Ala Lys Arg Gly Met Met Leu
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 Glu Gly Glu Phe Arg Tyr Leu Thr His Ser Ser Glu Gly Ile Val Asn
 370 375 380
 10
 Ala Ala Tyr Leu Asn Asp Lys Asp Asp His Arg Glu Gly Phe Pro Asp
 385 390 395 400
 15
 Tyr Ser Lys Asp Arg Trp Leu Tyr Gly Leu Lys Asn Thr Thr Gly Leu
 405 410 415
 20
 Asp Ser Arg Trp Leu Ala Glu Val Asp Tyr Thr Arg Ile Ser Asp Pro
 420 425 430
 25
 Tyr Tyr Phe Gln Asp Leu Asp Thr Asp Leu Gly Val Gly Ser Thr Thr
 435 440 445
 30
 Tyr Val Asn Gln Arg Gly Thr Leu Thr Tyr Arg Gly Asp Thr Phe Thr
 450 455 460
 35
 Gly Arg Leu Asn Ala Gln Ala Tyr Gln Leu Ala Thr Thr Thr Asp Val
 465 470 475 480
 40
 Thr Pro Tyr Asp Arg Leu Pro Gln Ile Thr Phe Asp Gly Phe Leu Pro
 485 490 495
 45
 Tyr Asn Pro Gly Gly Met Gln Phe Thr Tyr Gly Thr Glu Phe Val Arg
 500 505 510
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 Phe Asp Arg Asp Leu Asp Glu Asn Ile Tyr Phe Asn Asp Asp Gly Ser
 515 520 525
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 Ile Arg Gly Lys Arg Pro Asp Ala Ser Leu Gln Gly Leu Ala Arg Ala
 530 535 540
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 Thr Gly Asp Arg Met His Leu Glu Pro Gly Met Ser Leu Pro Met Thr
 545 550 555 560
 65
 Arg Ser Trp Gly Tyr Val Thr Pro Thr Leu Lys Tyr Leu Tyr Thr Lys
 565 570 575
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 Tyr Asp Leu Asp Leu Asp Ser Gln Gly Lys Thr Asp Leu Asn Lys Arg
 580 585 590
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 Asp Glu Ser Phe Asp Ser Asn Gln Asp Arg Ser Leu Pro Leu Val Lys

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	595					600					605					
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	610						615					620				
10	Pro	Phe	Arg	Gln	Thr	Leu	Glu	Pro	Arg	Ala	Met	Tyr	Leu	Tyr	Val	Pro
	625					630					635					640
15	Tyr	Lys	Asp	Gln	Asp	Ser	Leu	Pro	Val	Phe	Asp	Thr	Ser	Glu	Pro	Ser
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20	Phe	Ser	Tyr	Asp	Ser	Leu	Trp	Arg	Glu	Asn	Arg	Phe	Thr	Gly	Lys	Asp
				660					665					670		
25	Arg	Ile	Gly	Asp	Ala	Asn	Gln	Leu	Ser	Leu	Gly	Val	Thr	Ser	Arg	Phe
			675					680						685		
30	Ile	Glu	Glu	Asn	Gly	Phe	Glu	Arg	Ala	Ser	Ile	Ser	Ala	Gly	Gln	Ile
		690					695					700				
35	Tyr	Tyr	Phe	Arg	Asp	Arg	Arg	Val	Gln	Leu	Pro	Gly	Leu	Thr	Glu	Lys
	705					710					715					720
40	Asp	Leu	Lys	Arg	Leu	Asn	Leu	Asp	Pro	Ser	Gly	Leu	Asp	Asn	Asp	Ser
					725					730					735	
45	Trp	Arg	Ser	Pro	Tyr	Ala	Phe	Ala	Gly	Gln	Tyr	Arg	Phe	Asn	Arg	Asp
				740					745					750		
50	Trp	Arg	Ile	Asn	Ser	Asp	Phe	Asn	Trp	Asn	Pro	Asn	Thr	Ser	Arg	Thr
			755					760						765		
55	Glu	Ser	Gly	Ser	Ala	Ile	Phe	His	Tyr	Gln	Pro	Glu	Val	Asp	Pro	Gly
		770					775					780				
60	Lys	Val	Val	Asn	Val	Gly	Tyr	Arg	Tyr	Arg	Ala	Asp	Ala	Arg	Arg	Phe
	785					790					795					800
65	Asp	Ser	Ser	Arg	Gly	Thr	Phe	Arg	Tyr	Gly	Asn	Glu	Asn	Asp	Ile	Ile
					805					810					815	
70	Lys	Gln	His	Asp	Phe	Ser	Val	Ile	Trp	Pro	Leu	Val	Pro	Gln	Trp	Ser
				820					825					830		
75	Val	Leu	Ala	Arg	Trp	Gln	Tyr	Asp	Tyr	Asn	Lys	Asn	Arg	Thr	Leu	Glu
			835					840						845		

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Ala Phe Gly Gly Phe Glu Tyr Asp Ser Cys Cys Trp Lys Leu Arg Leu
850 855 860

5 Ile Asn Arg Tyr Trp Leu Asp Val Asp Asp Asp Ala Phe Leu Val Gln
865 870 875 880

10 Ser Glu Lys Ala Asp Arg Gly Ile Phe Leu Gln Ile Val Leu Lys Gly
885 890 895

15 Leu Gly Gly Ile Val Gly Asn Lys Thr Glu Met Phe Leu Asp Lys Gly
900 905 910

Ile Gln Gly Tyr Arg Gln Arg Glu Asp Gln Ala Met
915 920

20 <210> 12
<211> 340
<212> PRT
<213> Pseudomonas aeruginosa

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Met Lys Ala Thr Met Val Leu Thr Pro Leu Ala Leu Ala Met Ala Ala
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30 Val Leu Ser Val Ser Ala Tyr Ala Gly Asn Glu Gly Gly Trp His Pro
20 25 30

35 Pro Lys Pro Asn Pro Gln Ser Asn Asn Lys Gly Gly Ala Thr Ala Leu
35 40 45

40 Val Val Asp Thr Gln Gln Asn Tyr Asn Asn Lys Val Ser Asn Phe Gly
50 55 60

45 Thr Leu Asn Asn Ala Ser Val Ser Gly Ser Ile Lys Asp Ala Ser Gly
65 70 75 80

50 Asn Val Gly Val Asn Val Ala Ala Gly Asp Asn Asn Gln Gln Ala Asn
85 90 95

55 Ala Ala Ala Leu Ala Ser Ala Asp Ala Ser Phe Val Phe Gly Thr Ala
100 105 110

Thr Ala Ser Thr Ser Val Leu Gln Ser Gly Tyr Gly Asn Thr Leu Asn
115 120 125

Asn Tyr Ser Asn Pro Asn Thr Ala Ser Leu Ser Asn Ser Ala Asn Asn
130 135 140

55 Val Ser Gly Asn Leu Gly Val Asn Val Ala Ala Gly Asn Phe Asn Gln

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Ser Asn Phe Ser Ala Leu Gln Ser Gln Pro Asp Ala Thr Lys Val Ala
 35 40 45

5 Ala Leu Glu Thr Lys Asp Ala Gly Asp Trp Leu Ala Lys Ala Asp Lys
 50 55 60

10 Ala Tyr Gln Asp Gly Glu Asp Gln Arg Asp Val Asp Gln Leu Ala Tyr
 65 70 75 80

15 Leu Thr Asn Gln Arg Ile Glu Leu Ala Lys Gln Thr Ile Val Leu Arg
 85 90 95

Asn Ala Glu Ala Gln Leu Gln Asn Ala Ser Ala Gln Arg Ala Gln Ala
 100 105 110

20 Arg Leu Asp Ala Arg Thr Ala Gln Leu Asp Lys Leu Arg Ser Gln Leu
 115 120 125

25 Asn Ala Lys Gln Thr Ser Arg Gly Thr Met Val Thr Phe Gly Asp Val
 130 135 140

30 Leu Phe Asp Leu Asp Lys Ser Asp Leu Lys Pro Gly Ala Met Arg Asn
 145 150 155 160

Ile Gln Gln Leu Ala Glu Phe Leu Gln Gln Asn Pro Glu Arg Gln Val
 165 170 175

35 Ile Val Glu Gly Tyr Thr Asp Ser Thr Gly Ser Ala Asn Tyr Asn Gln
 180 185 190

40 Arg Leu Ser Glu Arg Arg Ala Asp Ser Val Arg Met Ala Leu Leu Ser
 195 200 205

45 Arg Gly Ile Ser Pro Glu Arg Val Ala Thr Arg Gly Tyr Gly Lys Glu
 210 215 220

Tyr Pro Val Ala Ser Asn Gly Thr Ser Ser Gly Arg Ala Met Asn Arg
 225 230 235 240

50 Arg Val Glu Val Thr Ile Ser Asn Asp Ala Lys Pro Val Ala Pro Arg
 245 250 255

Ser Ser Val Ser Gly
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55 <210> 14

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 <212> PRT
 <213> Pseudomonas aeruginosa

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15 Pro Ala Ala Ser Thr Gln Pro Ala Ala Pro Ala Ala Ala Pro Ala Ala
 35 40 45

20 Lys Val Asp Glu Ala Ala Ala Lys Ala Val Ile Lys Asn Tyr Ala Asp
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25 Leu Ala Glu Ala Thr Phe Ala Asp Ala Leu Ser Thr Ala Lys Asp Leu
 65 70 75 80

30 Gln Lys Ala Ile Asp Ala Phe Leu Ala Lys Pro Asp Ala Glu Thr Leu
 85 90 95

35 Lys Ala Ala Lys Glu Ala Trp Phe Ala Ala Arg Thr Pro Tyr Ser Gln
 100 105 110

40 Ser Glu Ala Phe Arg Phe Gly Asn Ala Ile Ile Asp Asp Trp Glu Gly
 115 120 125

45 Gln Val Asn Ala Trp Pro Leu Asp Glu Gly Leu Ile Asp Tyr Val Ala
 130 135 140

50 Lys Asp Tyr Gln His Ala Leu Gly Asn Pro Gly Ala Thr Ala Asn Ile
 145 150 155 160

55 Val Ala Asn Thr Glu Ile Gln Val Gly Glu Asp Lys Ile Asp Val Lys
 165 170 175

60 Glu Ile Thr Gly Glu Lys Leu Ala Ser Leu Asn Glu Leu Gly Gly Ser
 180 185 190

65 Glu Ala Asn Val Ala Thr Gly Tyr His Ala Ile Glu Phe Leu Leu Trp
 195 200 205

70 Gly Gln Asp Leu Asn Gly Thr Gly Pro Gly Ala Gly Asn Arg Pro Ala
 210 215 220

75 Thr Asp Tyr Ala Gln Gly Lys Asp Cys Thr Gly Gly His Cys Asp Arg
 225 230 235 240

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Arg Ala Ala Tyr Leu Lys Ala Val Thr Asp Leu Leu Val Ser Asp Leu
 245 250 255

5 Glu Tyr Met Ala Gly Gln Trp Lys Ala Gly Val Ala Asp Asn Tyr Arg
 260 265 270

10 Ala Lys Leu Glu Ala Glu Pro Val Asp Thr Gly Leu Arg Lys Met Phe
 275 280 285

15 Phe Gly Met Gly Ser Leu Ser Leu Gly Glu Leu Ala Gly Glu Arg Met
 290 295 300

Lys Val Ala Leu Glu Ala Asn Ser Thr Glu Asp Glu His Asp Cys Phe
 305 310 315 320

20 Ser Asp Asp Thr His His Thr Leu Phe Phe Asn Gly Lys Ser Ile Arg
 325 330 335

25 Asn Ile Tyr Leu Gly Glu Tyr Lys Arg Ile Asp Gly Ser Val Val Lys
 340 345 350

Gly Pro Ser Leu Ala Asp Leu Val Ala Lys Ala Asp Ala Ala Ala Asn
 355 360 365

30 Asp Thr Leu Lys Ala Asp Leu Ala Asp Thr Glu Ala Lys Leu Gln Ala
 370 375 380

35 Ile Val Asp Ser Ala Glu Lys Asp Gly Val His Phe Asp Gln Met Ile
 385 390 395 400

40 Ala Pro Asp Asn Lys Asp Gly Gln Gln Lys Ile Arg Asp Ala Ile Ala
 405 410 415

45 Ala Leu Val Lys Gln Thr Gly Ala Ile Glu Gln Ala Ala Gly Lys Leu
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Gly Ile Gln Asp Leu Lys Pro Asp Asn Ala Asp His Glu Phe
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50 <210> 15
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 <213> Pseudomonas aeruginosa

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Leu Leu Ser Pro Ser Leu Ala Leu Ala Gly Asn Ala Val Pro Leu Thr
 20 25 30
 5 Pro Thr Thr Ile Thr Ala Thr Arg Thr Glu Gln Ala Val Asp Ser Val
 35 40 45
 10 Pro Ser Thr Val Ser Val Gln Thr Arg Glu Gln Leu Asp Arg Gln Asn
 50 55 60
 Val Asn Asn Ile Lys Glu Leu Val Arg Tyr Glu Pro Gly Val Ser Val
 65 70 75 80
 15 Gly Gly Ala Gly Gln Arg Ala Gly Ile Thr Gly Tyr Asn Ile Arg Gly
 85 90 95
 20 Ile Asp Gly Asn Arg Ile Leu Thr Gln Ile Asp Gly Val Glu Leu Pro
 100 105 110
 Asn Asp Phe Phe Ser Gly Pro Tyr Ala Gln Thr His Arg Asn Tyr Val
 115 120 125
 25 Asp Pro Asp Ile Val Lys Arg Val Glu Ile Leu Arg Gly Pro Ala Ser
 130 135 140
 30 Ala Leu Tyr Gly Ser Asn Ala Ile Gly Gly Ala Val Ser Tyr Phe Thr
 145 150 155 160
 35 Leu Asp Pro Ser Asp Ile Ile Lys Asp Gly Lys Asp Val Gly Ala Arg
 165 170 175
 Leu Lys Ala Gly Tyr Glu Ser Ala Ser His Ser Trp Leu Thr Ser Ala
 180 185 190
 40 Thr Val Ala Gly Arg Ala Asp Asp Phe Asp Gly Leu Leu His Tyr Gly
 195 200 205
 45 Tyr Arg Gln Gly His Glu Thr Glu Ser Asn Gly Gly His Gly Gly Thr
 210 215 220
 Gly Leu Ser Arg Ser Glu Ala Asn Pro Glu Asp Ala Asp Ser Tyr Ser
 225 230 235 240
 50 Leu Leu Gly Lys Leu Gly Trp Asn Tyr Ala Glu Gly Ser Arg Phe Gly
 245 250 255
 55 Leu Val Phe Glu Lys Tyr Lys Ser Asp Val Asp Thr Asp Gln Lys Ser
 260 265 270

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Ala Tyr Gly Gly Pro Tyr Asp Lys Gly Lys Pro Ala Ile Pro Pro Ser
 275 280 285

5 Met Leu Pro Gly Gly Met Tyr Gln Trp Arg Lys Gly Asn Asp Thr Leu
 290 295 300

10 Thr Arg Glu Arg Tyr Gly Leu Glu His His Phe Leu Leu Asp Ser Gln
 305 310 315 320

15 Val Ala Asp Arg Ile Gln Trp Ser Leu Asn Tyr Gln Leu Ala Lys Thr
 325 330 335

20 Asp Gln Ala Thr Arg Glu Phe Tyr Tyr Pro Ile Thr Arg Lys Val Leu
 340 345 350

25 Arg Thr Arg Asp Thr Thr Tyr Lys Glu Arg Leu Trp Val Phe Asp Ser
 355 360 365

30 Gln Leu Asp Lys Ser Phe Ala Ile Gly Glu Thr Glu His Leu Leu Ser
 370 375 380

35 Tyr Gly Ile Asn Leu Lys His Gln Lys Val Thr Gly Met Arg Ser Gly
 385 390 395 400

40 Thr Gly Thr Asn Leu Asp Thr Gly Ala Asp Ser Pro Arg Asp Ala Leu
 405 410 415

45 Glu Arg Ser Ser Asp Phe Pro Asp Pro Thr Val Lys Thr Tyr Ala Leu
 420 425 430

50 Phe Ala Gln Asp Ser Ile Ser Trp Asn Asp Trp Thr Phe Thr Pro Gly
 435 440 445

55 Leu Arg Tyr Asp Tyr Thr Arg Met Glu Pro His Ile Thr Asp Glu Phe
 450 455 460

60 Leu Arg Thr Met Lys Gln Ser Gln Asn Thr Ala Val Asp Glu Ser Asp
 465 470 475 480

65 Lys Lys Trp His Arg Val Ser Pro Lys Phe Gly Val Thr Tyr Asp Phe
 485 490 495

70 Ala Gln His Tyr Thr Trp Tyr Gly Gln Tyr Ala Gln Gly Phe Arg Thr
 500 505 510

75 Pro Thr Ala Lys Ala Leu Tyr Gly Arg Phe Glu Asn Leu Gln Ala Gly

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	515					520					525					
5	Tyr	His	Ile	Glu	Pro	Asn	Pro	Asn	Leu	Lys	Pro	Glu	Lys	Ser	Gln	Ser
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10	Phe	Glu	Thr	Gly	Leu	Arg	Gly	Lys	Phe	Asp	Glu	Gly	Ser	Phe	Gly	Val
	545					550					555					560
15	Ala	Val	Phe	Tyr	Asn	Lys	Tyr	Arg	Asp	Phe	Ile	Asp	Glu	Asp	Ala	Leu
					565					570					575	
20	Asn	Thr	Asp	Ser	Thr	Gly	Gly	Asn	Gly	Gln	Thr	Phe	Gln	Ser	Asn	Asn
				580					585					590		
25	Ile	Glu	Arg	Ala	Val	Ile	Lys	Gly	Val	Glu	Leu	Lys	Gly	Arg	Leu	Glu
			595					600					605			
30	Leu	Gly	Ala	Phe	Gly	Ala	Pro	Gln	Gly	Leu	Tyr	Thr	Gln	Gly	Ser	Val
		610					615					620				
35	Ala	Tyr	Ala	Tyr	Gly	Arg	Asn	Lys	Asp	Asn	Gly	Glu	Pro	Ile	Asn	Ser
	625					630					635					640
40	Val	Asn	Pro	Leu	Thr	Gly	Val	Phe	Gly	Leu	Gly	Tyr	Asp	Glu	Ala	Asp
					645					650					655	
45	Gly	Asn	Tyr	Gly	Gly	Leu	Leu	Ser	Trp	Thr	Leu	Val	Lys	Arg	Lys	Asp
				660					665					670		
50	Arg	Val	Asp	Asp	Ser	Thr	Phe	His	Thr	Pro	Asp	Gly	Thr	Ala	Ser	Gln
			675					680					685			
55	Phe	Lys	Thr	Pro	Gly	Phe	Gly	Val	Leu	Asp	Leu	Ser	Ala	Tyr	Tyr	Arg
		690					695					700				
60	Leu	Ser	Lys	Asp	Leu	Thr	Leu	Asn	Ala	Gly	Leu	Tyr	Asn	Leu	Thr	Asp
	705					710					715					720
65	Lys	Lys	Tyr	Trp	Leu	Trp	Asp	Asp	Val	Arg	Gly	Tyr	Asp	Ser	Val	Gly
				725						730					735	
70	Glu	Ala	Ser	Ala	Leu	Ala	Pro	Ala	Asn	Ile	Asp	Arg	Leu	Ser	Gln	Pro
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75	Gly	Arg	Asn	Phe	Ala	Val	Asn	Leu	Val	Trp	Asp	Ile				
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 <211> 1088
 <212> PRT
 <213> Pseudomonas aeruginosa

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15
 Arg Val Ala Asn Gln Gln Leu Ala Gln Tyr Ala Thr Val Pro Ala Arg
 35 40 45

20
 Leu Glu Arg Ile Glu Phe Asn Pro Phe Ser Leu Glu Leu Thr Leu Trp
 50 55 60

25
 Gly Leu Arg Leu Gly Glu Glu Lys Asn Pro Gln Leu Ala Phe Arg Arg
 65 70 75 80

30
 Leu Tyr Ala Asn Leu Gln Leu Asp Ser Leu Trp Lys Arg Gln Leu His
 85 90 95

35
 Leu Ala Asp Val Glu Leu Glu Gly Pro His Thr Glu Leu Leu Phe Gly
 100 105 110

40
 Glu Lys Gly Gln Leu Asn Leu Ala Ser Leu Phe Arg Ile Pro Pro Ser
 115 120 125

45
 Glu Ser Pro Glu Pro Glu Gln Pro Ser Asp Pro Phe Pro Leu Arg Ile
 130 135 140

50
 Asp Arg Ile Gln Leu Ala Glu Gly Ser Leu His Phe Gln Asp Leu Arg
 145 150 155 160

55
 Pro Ser Glu Pro Val Asp Phe Ser Phe Asp Pro Leu Gly Phe Glu Leu
 165 170 175

60
 His Asn Leu Ser Thr Leu Pro Asp Asp Gly Ala Lys Met Thr Leu Val
 180 185 190

65
 Ala Thr Gly Pro Asn Gly Gly Arg Leu Asp Trp Glu Gly Asp Leu Thr
 195 200 205

70
 Leu Val Pro Ile Thr Ser Arg Gly His Leu Ser Val Lys Asp Ile Gln
 210 215 220

75
 Leu Lys Ala Trp Trp Pro Tyr Val Arg Asp Asn Ala Pro Leu Val Leu

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	225				230					235				240		
5	Glu	Asn	Gly	Val	Val	Ser	Leu	Ser	Ser	Asp	Tyr	Arg	Leu	Asp	Leu	Ser
					245					250					255	
10	Lys	Asp	Thr	Gln	Leu	Leu	Leu	Asp	Lys	Ala	Ala	Leu	Lys	Leu	Ala	Asp
				260					265					270		
15	Phe	Ser	Ile	Asn	Ser	Pro	Gln	Gly	Lys	Pro	Leu	Ala	Lys	Leu	Ala	Ser
			275					280						285		
20	Leu	Asp	Val	Ala	Ala	Thr	Thr	Leu	Asp	Leu	Ala	Lys	Gln	Glu	Val	Val
		290						295					300			
25	Leu	Gly	Glu	Val	Arg	Ser	Gln	Gly	Leu	Glu	Ala	Trp	Ala	Ala	Arg	Glu
	305					310						315				320
30	Lys	Asp	Gly	Gln	Leu	Asp	Trp	Gln	Lys	Leu	Phe	Ala	Asp	Phe	Thr	Pro
					325					330					335	
35	Pro	Pro	Arg	Lys	Ala	Pro	Ala	Pro	Lys	Pro	Ala	Glu	Asn	Thr	Asp	Pro
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40	Ala	Ala	Ala	Pro	Thr	Asp	Ala	Ala	Lys	Thr	Thr	Ser	Glu	Pro	Ala	Thr
			355						360					365		
45	Asp	Gly	Ala	Ala	Lys	Ala	Ala	Ala	Ile	Ala	Ser	Gly	Glu	Ala	Ser	Lys
		370							375				380			
50	Asp	Arg	Pro	Ala	Glu	Lys	Asp	Ala	Ser	Val	Ala	Glu	Thr	Glu	Arg	Ala
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55	Thr	Asp	Asp	Lys	Glu	Ser	Ala	Lys	Ala	Ala	Glu	Gly	Ala	Ala	Asp	Lys
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60	Val	Ala	Lys	Gln	Glu	Thr	Ser	Lys	Ala	Pro	Lys	Thr	Gly	Lys	Ala	Thr
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65	Gly	Gln	Glu	Thr	Ala	Lys	Thr	Ala	Glu	Ile	Asp	Lys	Ala	Ala	Ser	Asp
				435					440						445	
70	Ser	Pro	Gln	Gln	Leu	Ala	Asp	Thr	Ala	Lys	Thr	Pro	Pro	Pro	Glu	Ser
		450					455								460	
75	Thr	Lys	Ala	Ser	Ala	Glu	Thr	Pro	Ala	Lys	Pro	Trp	Asn	Ile	Val	Leu
	465					470						475				480

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Arg Asp Ala Gln Leu Arg Gly Tyr Lys Ala His Leu Val Asp Arg Gln
 485 490 495
 5 Pro Ala Thr Glu Val Pro Leu Glu Val Gly Pro Leu Asp Leu Asp Leu
 500 505 510
 10 Gln Asn Val Asp Ser Leu Gly Lys Thr Pro Phe Asp Leu Lys Leu Lys
 515 520 525
 Thr Gly Leu Gly Asn Arg Gly Gln Val Gln Ala Ser Gly Gln Val Val
 530 535 540
 15 Leu Asp Pro Val Ser Ala Arg Leu Lys Val Ser Thr Arg Asp Ile Asp
 545 550 555 560
 20 Leu Arg Val Ala Gln Ala Tyr Ile Ser Pro Phe Ile Arg Leu Glu Leu
 565 570 575
 Arg Ser Gly Phe Leu Gly Ser Glu Leu Ala Val Asp Leu Lys Ser Val
 580 585 590
 25 Glu Pro Leu Ala Phe Ser Val Asp Gly Ser Ala Glu Val Ser Gln Leu
 595 600 605
 30 His Thr Leu Asp Thr Ile Lys Asp Arg Asp Phe Val Lys Trp Thr Lys
 610 615 620
 35 Leu Thr Leu Asn Gly Leu Ala Tyr Arg His Glu Asp Ser Leu Ser Ile
 625 630 635 640
 Gln Ser Val Ser Phe Glu Glu Pro Tyr Ala Arg Phe Ile Ile Asn Glu
 645 650 655
 40 Asp Arg Ser Thr Asn Val Ser Glu Leu Ile Ile Pro Gln Pro Ala Ser
 660 665 670
 45 Ser Ser Gly Lys Thr Ala Ala Glu Ser Lys Asn Ala Pro Ala Ser Lys
 675 680 685
 50 Pro Leu Gly Ile His Ile Gly Gly Val Arg Ile Asn Asn Gly Ser Ala
 690 695 700
 Asn Phe Ala Asp Leu Thr Leu Met Pro Pro Phe Gly Thr Ala Ile Gln
 705 710 715 720
 55 Gln Leu Ser Gly Glu Val Gly Thr Leu Asp Thr Arg Asn Ser Gln Pro
 725 730 735

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	Ala	Lys	Val	Asp	Ile	Lys	Gly	Lys	Val	Asp	Lys	Tyr	Ala	Pro	Val	Thr
				740					745					750		
5	Ile	Ala	Gly	Glu	Leu	Asp	Pro	Phe	Asp	Pro	Leu	Lys	Lys	Leu	Asp	Ile
			755					760					765			
10	Thr	Thr	Ser	Phe	Lys	Arg	Val	Glu	Leu	Thr	Thr	Leu	Thr	Pro	Tyr	Ser
		770					775					780				
15	Gly	Lys	Phe	Ala	Gly	Tyr	Arg	Ile	Arg	Lys	Gly	Arg	Leu	Asn	Leu	Asp
	785					790					795					800
20	Leu	His	Tyr	Gln	Ile	Glu	Arg	Ser	Gln	Leu	Lys	Ala	Glu	Asn	Lys	Val
				805						810					815	
25	Leu	Leu	Glu	Gly	Leu	Gln	Leu	Gly	Glu	Lys	Val	Asp	Ser	Pro	Asp	Ala
				820					825					830		
30	Val	Asp	Leu	Pro	Val	Lys	Leu	Ala	Val	Ala	Leu	Leu	Lys	Asp	Thr	Lys
			835					840					845			
35	Gly	Asn	Ile	Asp	Ile	Gln	Leu	Pro	Val	Ala	Gly	Asp	Leu	Asn	Asn	Pro
		850					855					860				
40	Glu	Phe	Ser	Val	Met	Pro	Ile	Val	Trp	Gln	Thr	Leu	Arg	Asn	Leu	Val
	865					870					875					880
45	Leu	Arg	Ala	Val	Gln	Ala	Pro	Phe	Lys	Phe	Ile	Ala	Gly	Leu	Ala	Ala
					885					890					895	
50	Gly	Gly	Asn	Glu	Asp	Leu	Gly	Thr	Val	Pro	Phe	Ala	Ala	Gly	Ser	Asp
				900					905					910		
55	Glu	Leu	Thr	Pro	Glu	Ala	Gln	Ala	Asn	Leu	Asp	Lys	Leu	Ala	Asp	Ala
			915					920					925			
60	Leu	Lys	Glu	Arg	Pro	Ala	Leu	Arg	Leu	Glu	Val	Glu	Gly	Val	Ala	Ser
	930						935					940				
65	Ala	Ala	Ala	Asp	Gly	Pro	Ser	Ile	Gly	Ala	Lys	Arg	Leu	Glu	Leu	Glu
	945					950					955					960
70	Tyr	Gln	Asn	Thr	Tyr	Tyr	Arg	Met	Leu	Gln	Arg	Arg	Gly	Asp	Lys	Val
					965					970					975	
75	Pro	Ser	Asp	Ala	Lys	Gln	Leu	Glu	Val	Pro	Glu	Asn	Met	Gln	Ala	Pro
				980					985					990		

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Leu Leu Glu Gly Ile Tyr Arg Thr Arg Leu Lys Gln Gln Pro Pro Ala
 995 1000 1005

5 Glu Trp Lys Glu Leu Asp Ser Asp Glu Arg Thr Ala Lys Met Arg
 1010 1015 1020

10 Glu Ala Val Ile Ala Ser Trp Ala Lys Ser Gln Val Leu Leu Arg
 1025 1030 1035

15 Gln Ile Gly Gln Ala Arg Ala Thr Arg Ile Lys Asp Tyr Leu Val
 1040 1045 1050

Glu Lys Gly Gln Leu Pro Asp Asp Arg Ile Tyr Leu Ile Asp Val
 1055 1060 1065

20 Ser Phe Ala Glu Gly Glu Asp Lys Gly Asn Val Asp Thr Gln Leu
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25 His Leu Asp Ser Glu
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35 Ala Pro Ser Ala Phe Ala Glu Met Lys Ile Ala Val Leu Asn Tyr Gln
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40 Met Ala Leu Leu Glu Ser Asp Ala Ala Lys Gln Tyr Ala Val Asp Ala
 35 40 45

45 Glu Lys Lys Phe Gly Pro Gln Leu Asn Lys Leu Lys Asn Leu Glu Arg
 50 55 60

50 Asp Ala Lys Ala Leu Gln Asp Lys Leu Val Ser Asn Gly Ser Lys Met
 65 70 75 80

Ser Gln Gly Asp Arg Glu Lys Ala Glu Leu Asp Phe Lys Gln Lys Ala
 85 90 95

55 Arg Asp Phe Gln Phe Gln Ser Lys Glu Leu Asn Glu Ser Lys Ala Ala
 100 105 110

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Ala Asp Arg Asp Met Leu Lys Lys Leu Lys Pro Lys Leu Asp Gln Ala
115 120 125

5 Val Glu Glu Thr Ile Lys Lys Gly Gly Tyr Asp Met Val Ile Glu Arg
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10 Gly Ala Val Val Asp Val Lys Pro Gln Tyr Asp Ile Thr Arg Gln Val
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Ile Glu Arg Met Asn Gln Leu Arg
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15

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25 Leu Ala Ala Cys Ser Asp Ser Ala Pro Ser Ser Glu Glu Ile Ala Arg
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30 Leu Leu Ala Glu Arg Gly Phe Asp Lys Pro Ala Cys Ala Ser Ser Thr
35 40 45

35 Leu Phe Lys Thr Phe Pro Val Thr Leu Ser Asp Ser Phe Ser Gly Pro
50 55 60

Gly Pro Ala Lys Gly Asn Ala Ala Val Tyr Asp Ala Leu Val Gly Val
65 70 75 80

40 Gly Leu Leu Arg Arg Asp Gly Asp Ser Tyr Asp Leu Thr Pro Ala Gly
85 90 95

45 Arg Glu Asp Tyr Lys Pro Glu Ser Lys Ala Phe Cys Tyr Ser Ser Gly
100 105 110

Phe Asp Val Ser Val Arg Ser Val Asp Pro Ala Lys Pro Asp Asp Tyr
115 120 125

50 Gly Pro Ala Val Glu Lys Gly Trp Leu Val Thr Val Glu Val Lys Pro
130 135 140

55 Arg Glu Val Lys Asp Trp Ala Lys Asn Pro Glu Val Leu Lys Gln Ala
145 150 155 160

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Ser Leu Thr Thr Leu Gln Gln Ile Thr Gln Pro Gln Val Gly Gln Val
 165 170 175
 5 Ser Leu Val Lys Pro Arg Gly Glu Glu Gly Tyr Lys Leu Val Asn Thr
 180 185 190
 10 Arg Phe Ser Pro Arg Gln Gly Phe His Phe Asn Gln Ala Trp
 195 200 205
 15 <210> 19
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 25 Asp Ser Glu Leu Gln Phe Leu Ala Arg Thr Tyr Tyr Phe Asn Arg Asp
 35 40 45
 30 Tyr Arg Asp Ser Pro Asn Asn Ala Gly Arg Asn Arg Phe Lys Pro Arg
 50 55 60
 35 Ser Glu Arg Asn Gly Tyr Arg Glu Glu Ala Thr Gln Gly Leu Arg Leu
 65 70 75 80
 40 Gln Phe Ala Ser Gly Tyr Thr Pro Gly Ser Leu Gly Phe Gly Leu Asp
 85 90 95
 45 Ala His Ala Met Leu Gly Leu Gln Leu Asp Ser Gly Gly Gly Arg Thr
 100 105 110
 50 Gly Thr Gly Asn Leu Pro Val Gly Ala Asp Gly His Pro Asp His Arg
 115 120 125
 55 Tyr Gly Lys Val Gly Gly Ala Leu Arg Leu Arg His Gly Glu Thr Arg
 130 135 140
 60 Leu Lys Tyr Gly Gln Thr Thr Thr Ser Ala Pro Val Phe Ala Ala Ser
 145 150 155 160
 65 Ser Asn Arg Thr Leu Ala Gly Met Ala Tyr Gly Leu Leu Leu Glu Asp
 165 170 175
 70 Arg Ser Phe Asp Gly Leu Leu Leu Glu Gly Gly Arg Phe Thr Ala Ala

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				180					185					190			
5	Ser	Gly	Pro	Gly	Glu	Ser	Lys	Val	Arg	Gly	Asp	Ile	Ser	Thr	Val	Tyr	
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10	Gly	Arg	Leu	Gly	Ala	Tyr	Pro	Val	Arg	Leu	Asp	Ala	Val	Gly	Phe	Leu	
		210					215					220					
15	Gly	Gly	Gln	Trp	Gln	Ala	Thr	Glu	Arg	Leu	Gln	Leu	Ser	Leu	Tyr	Ala	
		225				230					235					240	
20	Ser	Arg	Phe	Asp	Asp	Ile	Trp	Gln	Gln	Ala	Tyr	Phe	Gly	Ala	Ser	His	
				245						250					255		
25	Arg	Gln	Pro	Leu	Gly	Gly	Glu	Arg	Ala	Leu	Arg	Val	Asp	Leu	Asp	Ala	
				260					265					270			
30	Tyr	Arg	Thr	Arg	Asp	Ser	Gly	Gln	Ser	Arg	Phe	Gly	Arg	Ile	Asp	Thr	
			275					280					285				
35	Leu	Thr	Ser	Ser	Leu	Ala	Leu	Gly	Tyr	Glu	His	Gly	Pro	Gln	Arg	Ile	
		290					295					300					
40	Thr	Leu	Ala	Tyr	Gln	Arg	Val	His	Gly	Glu	Gln	Pro	Phe	Asp	Tyr	Met	
		305				310					315					320	
45	Ala	Phe	Gly	Asp	Gly	Arg	Ser	Ser	Ala	Ser	Met	Val	Leu	Ala	Asn	Ser	
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50	Val	Gly	Tyr	Ser	Asp	Phe	Asn	Gly	Pro	Gly	Glu	Arg	Ser	Trp	Gln	Leu	
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55	Arg	Tyr	Asp	Leu	Asp	Leu	Gly	Ala	Leu	Gly	Leu	Pro	Gly	Leu	Ser	Leu	
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60	His	Ala	Leu	His	Ala	Arg	Gly	Arg	Ala	Gly	Ala	Ser	Ala	Ser	Ser	Ala	
		370					375					380					
65	Ala	Glu	Ser	Ile	Tyr	Ala	Gly	Leu	Tyr	Gly	Arg	Asp	Gly	Arg	His	Arg	
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70	Glu	Asn	Asp	Leu	Gly	Phe	Ala	Tyr	Arg	Val	Lys	Ala	Gly	Pro	Leu	Ala	
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75	Gly	Leu	Ala	Leu	Arg	Ala	Ser	Gln	Ala	Trp	His	Arg	Gly	Asn	Ala	Ser	
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 5 Arg Ser Ile Trp
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 Gln Gln Leu Gln Val Gln Ala Cys Arg Ala Val Gly Ser Leu Leu Leu
 25 35 40 45
 Leu Arg Gly Glu Gly Phe Gln Glu Gln His Ala Ala Gln Leu Glu Lys
 50 55 60
 Asp Leu Ala Ser Leu Asp Arg Ala Leu Ala Ala Ala Pro Glu Gly Val
 30 65 70 75 80
 Leu Leu Arg Gln Gly Glu Lys Thr Leu Val Ala Arg Ile Arg Glu Gly
 85 90 95
 Ala Ala Tyr Gly Pro Arg Glu Glu Asp Leu Pro Trp Arg Tyr Pro Gln
 35 100 105 110
 Gln Leu Ser Arg Ala Leu Arg Asp Phe Leu Asn Leu Val Glu Arg Gln
 40 115 120 125
 Val Pro Pro Pro Pro Pro Gly Gln Pro Leu Pro Leu Trp Gln Leu Pro
 130 135 140
 Val Arg Val Glu Tyr Leu Ser Leu Gln Tyr Leu Ala Arg Ala Tyr Leu
 45 145 150 155 160
 Gly Gly Leu Glu Thr Ala Arg Glu Gln Pro Arg Asp Tyr Leu Gly Gln
 50 165 170 175
 Asp Glu Ser Val Leu Val Pro Leu Ile Asp Arg Arg Ile Ala Leu Leu
 180 185 190
 55 Val Ala Gln Ser Ala Asn Pro Ala Gly Leu Lys Lys Leu Glu Asn Arg

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	195		200		205														
5	Trp	Glu	Tyr	Leu	Ser	Gln	Ala	Leu	Arg	Asp	Leu	Asn	Ser	Lys	Ser	Ser			
	210						215					220							
10	Ala	Leu	Val	Ser	Ala	Ser	Gly	Arg	Pro	Trp	Ala	Pro	Ile	Ile	Val	Asp			
	225					230					235					240			
15	Arg	His	Ala	Arg	Ala	Leu	Ser	Glu	Ser	Leu	Met	Arg	Leu	Ser	Ala	Glu			
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25	Leu	Ser	Gly	Cys	Gly	Tyr	Asn	Ala	Met	Gln	Ala	Gly	Asp	Glu	Gln	Val			
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30	Lys	Ala	Ala	Trp	Ser	Glu	Val	Leu	Asn	Gln	Tyr	Gln	Arg	Arg	Ala	Asp			
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35	Leu	Val	Pro	Asn	Leu	Val	Ser	Thr	Val	Lys	Gly	Tyr	Ala	Ser	His	Glu			
		50					55					60							
40	Ala	Ser	Val	Leu	Thr	Gln	Val	Thr	Glu	Ala	Arg	Ala	Lys	Val	Gly	Ser			
	65					70					75					80			
45	Val	Gln	Leu	Asn	Ala	Asp	Gln	Leu	Asp	Asp	Glu	Gln	Ala	Val	Gln	Arg			
					85					90					95				
50	Phe	Gln	Lys	Ala	Gln	Gly	Glu	Leu	Ser	Ser	Ala	Leu	Ser	Arg	Leu	Leu			
				100					105					110					
55	Val	Val	Thr	Glu	Asn	Tyr	Pro	Gln	Leu	Lys	Ala	Asp	Gly	Leu	Phe	Lys			
			115					120					125						
60	Asp	Leu	Leu	Thr	Gln	Leu	Glu	Gly	Thr	Glu	Asn	Arg	Ile	Ala	Val	Ala			
		130					135					140							
65	Arg	Gly	Arg	Tyr	Val	Lys	Ser	Val	Gln	Glu	Tyr	Asn	Val	Leu	Leu	Arg			
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Ala Asn Phe Ser Val Glu Asn Glu Ala Ala Ile Ser Thr Ala Pro Lys
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5 Val Asp Phe Gly Asn Pro Gln Pro Ala Gln
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25 Arg His Tyr Arg Gly Gln Pro Tyr Gly Tyr Ala Tyr Glu Val Pro Arg
 35 40 45

30 Tyr Arg Val Tyr Asp Asp Gly Trp Arg Ser Glu Arg Arg Tyr Tyr Ser
 50 55 60

35 Thr Arg Tyr Tyr Asp Gln Arg Tyr Tyr Pro Ala Pro Arg Arg Tyr Asp
 65 70 75 80

40 Gly His Arg Asp Tyr Arg Arg Glu Gln Tyr Arg Tyr Gln Gln Arg Tyr
 85 90 95

45 His Glu Ser Arg Pro Ala His Arg Gly Glu Arg His Pro Gly Asn Trp
 100 105 110

50 Gln Arg Gly Gly Gln Pro Gln Trp Arg Gly His Ser Pro Gln Arg Trp
 115 120 125

55 Gln Gln His Gly Arg Gln Asp Arg Pro Gly His Gln Gly Gln Gln Gly
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Gly Thr Pro Arg Trp Arg Asn
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60 <210> 23
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	Gln	Asn	Ser	Glu	Leu	Asn	Ala	Phe	Leu	Gly	Gln	Ile	Asp	Gln	Leu	Asn
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	Ser	Leu	Leu	Ala	Asp	Asn	Thr	Thr	Gly	Val	Ser	Pro	Ala	Met	Gln	Arg
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	Phe	Phe	Ser	Ala	Leu	Gln	Thr	Ala	Ala	Gln	Asn	Pro	Ser	Ser	Thr	Glu
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	Gln	Leu	Gly	Ala	Leu	Thr	Ser	Gln	Val	Asn	Asn	Leu	Ser	Gln	Ser	Val
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40	Ala	Glu	Tyr	Asn	Asp	Ala	Ile	Ala	Lys	Ala	Lys	Ser	Ala	Gly	Ala	Val
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45	Pro	Asn	Asp	Leu	Leu	Asp	Ala	Arg	Asp	Glu	Ala	Val	Arg	Lys	Leu	Ser
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	Glu	Met	Val	Gly	Val	Thr	Ala	Val	Thr	Gln	Asp	Asp	Asn	Ser	Val	Ser
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	Leu	Phe	Ile	Gly	Ser	Gly	Gln	Pro	Leu	Val	Val	Gly	Asn	Thr	Val	Ser
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55	Thr	Leu	Ser	Val	Val	Pro	Gly	Leu	Asp	Asp	Pro	Thr	Arg	Tyr	Gln	Val
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Gln Leu Thr Leu Gly Asp Ser Thr Gln Asn Val Thr Arg Leu Val Ser
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 5 Gly Gly Gln Met Gly Gly Leu Leu Ala Tyr Arg Asp Thr Val Leu Asp
 275 280 285
 10 Ser Ser Tyr Asn Lys Leu Gly Gln Leu Ala Leu Thr Phe Ala Asp Thr
 290 295 300
 15 Val Asn Lys Gln Leu Gly Gln Gly Leu Asp Leu Ala Gly Lys Ala Gly
 305 310 315 320
 20 Ala Asn Leu Phe Gly Asp Ile Asn Asp Pro Asp Ile Thr Ala Leu Arg
 325 330 335
 25 Val Leu Ala Lys Asn Gly Asn Thr Gly Asn Val His Ala Asn Leu Asn
 340 345 350
 30 Ile Thr Asp Thr Ser Lys Leu Asn Ser Ser Asp Phe Arg Leu Asp Phe
 355 360 365
 35 Asp Gly Thr Asn Phe Thr Ala Arg Arg Leu Gly Asp Asp Ala Ser Met
 370 375 380
 40 Gln Val Thr Val Ser Gly Thr Gly Pro Tyr Thr Leu Ser Phe Lys Asp
 385 390 395 400
 45 Ala Asn Gly Val Asp Gln Gly Phe Ser Val Thr Leu Asp Gln Leu Pro
 405 410 415
 50 Ala Ala Gly Asp Arg Phe Thr Leu Gln Pro Thr Arg Arg Gly Ala Ser
 420 425 430
 55 Asp Ile Glu Thr Thr Leu Lys Asn Ala Ser Gln Leu Ala Phe Ala Gly
 435 440 445
 60 Ser Ala Arg Ala Glu Ala Thr Thr Asn Asn Arg Gly Ser Gly Ala Ile
 450 455 460
 65 Gly Gln Pro Asn Leu Val Asp Gly Pro Ser Pro Ile Asp Pro Ala Val
 465 470 475 480
 70 Leu Gln Asn Ala Phe Gly Ala Asn Gly Leu Pro Leu Ser Ala Thr Val
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 75 Ser Ala Asp Gly Lys Thr Tyr Thr Met Thr Ser Pro Leu Pro Ala Gly
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Trp Ser Tyr Val Asp Lys Asp Gly Asn Ala Leu Pro Gly Ser Pro Thr
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5 Leu Asn Ser Gly Thr Ser Asn Ser Val Arg Met Ala Tyr Thr Asp Pro
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10 Gly Ser Gly Gln Thr Tyr Thr Tyr Glu Phe Asn Leu Ser Asn Val Pro
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Gln Thr Gly Asp Ser Phe Thr Leu Ser Phe Asn Lys Asp Gly Ile Ala
565 570 575

15 Asp Asn Arg Asn Ala Leu Asn Leu Asn Ala Leu Gln Thr Lys Pro Thr
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20 Val Gly Gly Thr Asp Ser Thr Gly Ser Thr Tyr Asn Asp Ala Tyr Gly
595 600 605

25 Gly Leu Val Glu Arg Val Gly Thr Leu Thr Ala Gln Ala Arg Ala Ser
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Ala Asp Ala Ser Gln Thr Val Leu Lys Gln Ala Gln Asp Ser Arg Asp
625 630 635 640

30 Ser Leu Ser Gly Val Ser Leu Asp Glu Glu Ala Ala Asn Leu Ile Gln
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35 Phe Gln Gln Tyr Tyr Ser Ala Ser Ala Gln Val Ile Gln Val Ala Arg
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45 <213> Pseudomonas aeruginosa

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55 Lys Leu Ala Thr Ser Pro Thr Arg Ser Met Ala Gln Gly Leu Val Thr
35 40 45

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Pro Gly Ser Ser Gly Ser Phe His Gly Gly Leu Asp Leu Ser His Glu
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 5 Ser Gly Trp Tyr Ile Gly Asn Trp Thr Ser Asn Leu Asp Pro Gly Lys
 65 70 75 80
 10 Pro Thr Glu Ile Asp Ser Tyr Ala Gly Phe Lys Arg Pro Leu Asn Asn
 85 90 95
 Arg Leu Gly Tyr Glu Met Gly Leu Ile Arg Tyr Ser Arg Pro Glu Gln
 100 105 110
 15 Pro Ala Asn Asp Ala Ala Glu Leu Tyr Gly Gly Leu Ser Ile Phe Gly
 115 120 125
 20 Ser Arg Leu Gly Ala Ala Leu Ser Ser Asp Pro Gly Arg Asn Asp Thr
 130 135 140
 Thr Leu Phe Ala Asp Leu Gly Val Asn Pro Pro Phe Gly Phe Asp Val
 145 150 155 160
 25 Thr Leu Lys Tyr Gly Asn His Arg Leu Asp Asn Pro Ala Ser Leu Ser
 165 170 175
 30 Gly Gly Gly Tyr Val Ser Val Phe Asn Asp Trp Ser Val Asn Leu Ser
 180 185 190
 Arg Pro Trp Leu Gly Ile Asp Leu Asn Leu Ser Tyr Ser Gly Thr Ser
 195 200 205
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 40 Asp Thr Thr Phe Met Leu Lys Ala Ser Arg Pro Phe Phe
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5	Asp	Leu	Tyr	Leu	Thr	Ser	Ala	Ser	Gly	Ala	Ile	Gln	Lys	Gly	Thr	Asn			
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10	Thr	Lys	Val	Ala	Leu	Glu	Pro	Ala	Thr	Ser	Tyr	Met	Lys	Ala	Tyr	Tyr			
	65					70					75					80			
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20	Pro	Pro	Val	Leu	Asp	Pro	Arg	Arg	Ala	Thr	Tyr	Val	Arg	Glu	Ala	Thr			
				100					105					110					
25	Thr	Asp	Gln	Asn	Gly	Arg	Phe	Asp	Phe	Asp	His	Ile	Pro	Asn	Gly	Thr			
			115					120					125						
30	Tyr	Tyr	Ile	Ser	Ser	Glu	Leu	Thr	Trp	Ser	Ala	Gln	Ser	Asp	Gly	Lys			
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55	Ala	Ser	Ala	Met	Asn	Ala	Phe	Ala	Gln	Gly	Gln	Asn	Ser	Val	Glu	Ile			
				20					25					30					
60	Glu	Ala	Phe	Gly	Lys	Arg	Tyr	Phe	Thr	Asp	Ser	Val	Arg	Asn	Met	Lys			
			35					40					45						
65	Asn	Ala	Asp	Leu	Tyr	Gly	Gly	Ser	Ile	Gly	Tyr	Phe	Leu	Thr	Asp	Asp			
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75	Tyr	Glu	Thr	Gly	Asn	Lys	Lys	Val	His	Gly	Asn	Leu	Thr	Ser	Leu	Asp			
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Ala Ile Tyr His Phe Gly Thr Pro Gly Val Gly Leu Arg Pro Tyr Val
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5 Ser Ala Gly Leu Ala His Gln Asn Ile Thr Asn Ile Asn Ser Asp Ser
115 120 125

10 Gln Gly Arg Gln Gln Met Thr Met Ala Asn Ile Gly Ala Gly Leu Lys
130 135 140

15 Tyr Tyr Phe Thr Glu Asn Phe Phe Ala Lys Ala Ser Leu Asp Gly Gln
145 150 155 160

Tyr Gly Leu Glu Lys Arg Asp Asn Gly His Gln Gly Glu Trp Met Ala
165 170 175

20 Gly Leu Gly Val Gly Phe Asn Phe Gly Gly Ser Lys Ala Ala Pro Ala
180 185 190

25 Pro Glu Pro Val Ala Asp Val Cys Ser Asp Ser Asp Asn Asp Gly Val
195 200 205

Cys Asp Asn Val Asp Lys Cys Pro Asp Thr Pro Ala Asn Val Thr Val
210 215 220

30 Asp Ala Asn Gly Cys Pro Ala Val Ala Glu Val Val Arg Val Gln Leu
225 230 235 240

35 Asp Val Lys Phe Asp Phe Asp Lys Ser Lys Val Lys Glu Asn Ser Tyr
245 250 255

40 Ala Asp Ile Lys Asn Leu Ala Asp Phe Met Lys Gln Tyr Pro Ser Thr
260 265 270

Ser Thr Thr Val Glu Gly His Thr Asp Ser Val Gly Thr Asp Ala Tyr
275 280 285

45 Asn Gln Lys Leu Ser Glu Arg Arg Ala Asn Ala Val Arg Asp Val Leu
290 295 300

50 Val Asn Glu Tyr Gly Val Glu Gly Gly Arg Val Asn Ala Val Gly Tyr
305 310 315 320

Gly Glu Ser Arg Pro Val Ala Asp Asn Ala Thr Ala Glu Gly Arg Ala
325 330 335

55 Ile Asn Arg Arg Val Glu Ala Glu Val Glu Ala Glu Ala Lys

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	Met	Asp	Asp	Pro	Arg	Asn	Ala	Gln	Met	Leu	Asp	Leu	Val	Asp	Gln	Ala	
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20	Leu	Lys	Gly	Asn	Met	Ala	Val	Val	Leu	Val	Ala	Asp	Val	Met	Pro	His	
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	Lys	Ser	Leu	Ser	Asp	Ala	Leu	Thr	Met	Thr	Gln	Trp	Thr	Pro	Thr	Ala	
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	Ile	Trp	Glu	Tyr	Glu	Lys	Asp	Pro	Lys	Val	Thr	Phe	Gly	Arg	Lys	Phe	
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30	Gln	Thr	Asn	Ala	Leu	Gln	Arg	Lys	Pro	Asp	Glu	Thr	Tyr	Leu	Phe	Lys	
				100					105					110			
	Ala	Phe	Glu	Val	His	Ile	Leu	Pro	Pro	Gly	Lys	Tyr	Leu	Leu	Thr	Gly	
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	Gly	Asp	Asp	Tyr	Gln	Ile	His	Gly	Leu	Leu	Asp	Gln	Val	Gly	Ala	Arg	
40		130					135					140					
	Ser	Gly	Pro	Pro	Gly	Ser	Gly	His	Gly	Ala	Asn	Gly	Thr	Ala	Tyr	Leu	
	145					150					155					160	
45	Ser	Pro	Glu	Leu	Tyr	Arg	Glu	Tyr	Tyr	Arg	Glu	Glu	Val	Trp	Lys	Asp	
					165					170					175		
	Ala	Thr	Tyr	Gly	Ser	Glu	Ile	Lys	Thr	Glu	Lys	Val	Cys	Thr	Ala	Val	
50			180						185					190			
	His	Val	Ala	Ser	Gly	Ala	Cys	Val	Ser	Trp	Gly	Glu	Gln	Gln	Tyr	Thr	
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55	Gln	Thr	Thr	Gln	Gly	Ser	Gln	Ala	Gly	Tyr	Tyr	Gln	Gln	Thr	Asp	Ser	
		210					215					220					

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Arg Asp Val Pro Ser Ile Lys Val Gln Ala Arg Leu Pro Val Asp Lys
 225 230 235 240

5
 Ala Leu Ala Ser Phe Thr Val Gln Gly Gly Gln Leu Leu Leu Ala Pro
 245 250 255

10
 Arg Met His Leu Lys Thr Pro Gly Tyr Lys Tyr Gln Gln Ser Lys Cys
 260 265 270

15
 Arg Ala Ile Asp Pro Lys Lys Ile Glu Cys Pro Leu Glu Asn Leu Thr
 275 280 285

20
 Val Tyr Thr Trp Pro Ala Pro Met Asp Phe Ser Gln Ser Leu Ile Ala
 290 295 300

25
 Gln Arg Ala Leu Ser Asp Lys His Arg Gln Leu Leu Ser Arg Leu Gln
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 Trp Gly Val Pro Leu Ser Leu Lys
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<210> 28
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50
 Val Glu Ala Gly Arg Pro Gly Asp Pro Ala Ser Trp Arg Ser Ala Glu
 35 40 45

55
 Tyr Gln Gln Asp Trp Gly Leu Glu Arg Met Arg Ala Asp Gln Ala Tyr
 50 55 60

60
 Ala Ala Gly Ile Asp Gly Gln Gly Val Lys Ile Gly Glu Met Asp Ser
 65 70 75 80

65
 Gly Phe Asp Pro Ser His Pro Asp Thr Pro Ala Ser Arg Tyr Gln Pro
 85 90 95

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Val Thr Ala Ser Gly Thr Tyr Val Asp Gly Thr Pro Phe Ser Val Ser
 100 105 110

5 Gly Ala Met Asn Gly Asn Asn Asp Ser His Gly Thr His Val Gly Gly
 115 120 125

10 Thr Leu Gly Ala Ser Arg Asp Gly Val Gly Met His Gly Val Ala Tyr
 130 135 140

Ala Ala Gln Val Tyr Val Ala Asn Thr Asn Gln Asn Asp Ser Phe Leu
 145 150 155 160

15 Phe Gly Pro Thr Pro Asp Pro Asn Tyr Phe Lys Ala Ala Tyr Gln Ala
 165 170 175

20 Leu Ala Asp Ala Gly Val Arg Ala Ile Asn Asn Ser Trp Gly Ser Gln
 180 185 190

25 Pro Lys Asp Val Ser Tyr Glu Thr Leu Asp Gly Leu His Ala Ala Tyr
 195 200 205

Ala Gln His Tyr Gly Arg Ser Thr Trp Leu Asp Ala Ala Ala Gly Val
 210 215 220

30 Ser Arg Gln Gly Val Ile Asn Val Phe Ser Ala Gly Asn Ser Gly Tyr
 225 230 235 240

35 Ala Asn Ala Ser Val Arg Ser Ala Leu Pro Tyr Phe Gln Pro Asp Leu
 245 250 255

40 Glu Gly His Trp Leu Ala Val Ser Gly Leu Asp Gln Gln Asn Gly Gln
 260 265 270

Arg Tyr Asn Arg Cys Gly Ile Ala Lys Tyr Trp Cys Ile Thr Thr Pro
 275 280 285

45 Gly Arg Leu Ile Asn Ser Thr Met Pro Gly Gly Gly Tyr Ala Asn Lys
 290 295 300

50 Ser Gly Thr Ser Met Ala Ala Pro His Ala Thr Gly Ala Leu Ala Leu
 305 310 315 320

Val Met Gln Arg Tyr Pro Tyr Leu Asn Asn Glu Gln Ala Leu Gln Val
 325 330 335

55 Leu Leu Thr Thr Ala Thr Gln Leu Asp Gly Thr Pro Thr Gly Ala Pro
 340 345 350

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Thr Asp Thr Val Gly Trp Gly Val Pro Asp Leu Gly Arg Ala Met His
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5 Gly Pro Gly Gln Leu Leu Gly Arg Phe Glu Ala Asn Leu Pro Ala Gly
 370 375 380

10 Leu Arg Asp Glu Trp Ser Asn Pro Ile Ser Asp Ser Ala Leu Leu Gln
 385 390 395 400

15 Arg Gln Ala Glu Asp Ala Ala Glu His Ala Ala Trp Gln Arg Thr Leu
 405 410 415

20 Lys Asp Lys Gly Trp Glu Asn Gly Leu Pro Ala Gly Ala Ser Gln Gln
 420 425 430 435

25 Glu Arg Thr Asp Tyr Ala Ile Gly Met Ala Arg Asp Gln Ala Ala Ala
 435 440 445

30 Gln Arg Gln Tyr Gln Gly Ser Leu Val Lys Ala Gly Ala Gly Ser Leu
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35 Val Leu Ser Gly Asp Ser Thr Tyr Arg Gly Pro Thr Leu Val Asp Gly
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40 Gly Leu Leu Ser Val Asp Gly Ser Leu Leu Ser Ala Val Glu Val Asn
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45 Ala Gly Gly Thr Leu Gly Gly Ser Gly Arg Ile Gly Gly Leu Leu Ala
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50 Arg Ser Gly Gly Thr Val Ala Ala Gly Asn Ser Ile Gly Thr Leu Glu
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55 Val Ala Gly Asp Leu Arg Phe Glu Ser Gly Ser Thr Tyr Ala Val Glu
 530 535 540

60 Leu Ser Glu Ser Ala Ser Asp Arg Ile Val Ala Ser Gly Lys Ala Ser
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65 Ile Ala Gly Gly Asn Val Thr Leu Ala Met Glu Asn Ser Pro Asp Leu
 565 570 575

70 Leu Ser Gln Ser Gln Val Glu Ser Leu Val Gly Arg Arg Tyr Asp Ile
 580 585 590

75 Leu Asp Ala Ala Gly Gly Ile Asp Gly Arg Phe Asp Ala Val Leu Pro

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15	Thr	Pro	Asn	Gln	Ala	Ala	Val	Ala	Gly	Ala	Val	Glu	Thr	Leu	Gly	Ala
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20	Gly	Asn	Pro	Val	Tyr	Glu	Ser	Leu	Leu	Leu	Ser	Glu	Asn	Ala	Ala	Thr
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25	Ala	Gln	Arg	Ala	Phe	Gln	Gln	Leu	Ser	Gly	Glu	Ile	Tyr	Pro	Ala	Leu
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40	Glu	Gly	Trp	Phe	Lys	Ala	Leu	Gly	Ser	Trp	Gly	Lys	Ser	Ala	Asp	Gly
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45	Ser	His	Gly	Ser	Glu	Gly	Tyr	Arg	His	Ser	Val	Gly	Gly	Phe	Leu	Leu
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70	Glu	Val	Lys	Arg	Asp	Leu	Gln	Tyr	Gly	Ala	Val	Ala	Gly	Lys	Gln	Lys
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5 Tyr Val His Val Ala Ser Asp Asp Phe Arg Glu Arg Gly Ser Ala Ala
 865 870 875 880

Ala Leu Glu Gly Gly Asp Asp Asn Leu Asp Ala Ala Phe Thr Thr Leu
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Gly Leu Arg Ala Lys Arg His Phe Glu Leu Asp Ala Gly Arg Arg Leu
 900 905 910

15 Ala Leu Ser Gly Thr Leu Gly Trp Arg His Asn Leu Ser Asp Thr Thr
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Pro Gln Arg His Leu Ala Phe Ala Ser Gly Ser Gln Pro Phe Ser Val
 20 930 935 940

Glu Ser Val Ala Leu Ser Arg Asp Ala Ala Leu Leu Gly Val Asp Ala
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Ser Leu Ala Val Asn Arg Glu Val Ser Val Arg Leu Gly Tyr Asn Gly
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Trp Arg Phe
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50 Leu Phe Lys Gly Gln Arg Gly Val Ala Thr His Val Val Ala Ala Thr
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Thr Asn Gly Thr Ser Gly Asn Asn Thr Phe Gly Met Thr Thr Gly Thr
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55 Asn Gly Cys His Thr Asn Gly Ala Leu Ser Tyr Gly Gly Lys Pro Leu

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60	Glu	Asp	Ser	Leu	Tyr	Ser	Leu	Leu	Val	Ala	Glu	Leu	Ala	Gly	Gln	Arg																			
	65					70					75																								
65	Asn	Arg	Phe	Asp	Ile	Ala	Leu	Ser	Asn	Tyr	Val	Val	Gln	Ala	Gln	Lys																			
					85					90					95																				
70	Thr	Arg	Asp	Pro	Gly	Val	Ser	Glu	Arg	Ala	Phe	Arg	Ile	Ala	Glu	Tyr																			
				100					105					110																					
75	Leu	Gly	Ala	Asp	Gln	Glu	Ala	Leu	Asp	Thr	Ser	Leu	Leu	Trp	Ala	Arg																			
			115					120					125																						

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Ser Ala Pro Asp Asn Leu Asp Ala Gln Arg Ala Ala Ala Ile Gln Leu
 130 135 140

5
 Ala Arg Ala Gly Arg Tyr Glu Glu Ser Met Val Tyr Met Glu Lys Val
 145 150 155 160

10
 Leu Asn Gly Gln Gly Asp Thr His Phe Asp Phe Leu Ala Leu Ser Ala
 165 170 175

15
 Ala Glu Thr Asp Pro Asp Thr Arg Ala Gly Leu Leu Gln Ser Phe Asp
 180 185 190

20
 His Leu Leu Lys Lys Tyr Pro Asn Asn Gly Gln Leu Leu Phe Gly Lys
 195 200 205

25
 Ala Leu Leu Leu Gln Gln Asp Gly Arg Pro Asp Glu Ala Leu Thr Leu
 210 215 220

30
 Leu Glu Asp Asn Ser Ala Ser Arg His Glu Val Ala Pro Leu Leu Leu
 225 230 235 240

35
 Arg Ser Arg Leu Leu Gln Ser Met Lys Arg Ser Asp Glu Ala Leu Pro
 245 250 255

40
 Leu Leu Lys Ala Gly Ile Lys Glu His Pro Asp Asp Lys Arg Val Arg
 260 265 270

45
 Leu Ala Tyr Ala Arg Leu Leu Val Glu Gln Asn Arg Leu Asp Asp Ala
 275 280 285

50
 Lys Ala Glu Phe Ala Gly Leu Val Gln Gln Phe Pro Asp Asp Asp Asp
 290 295 300

55
 Leu Arg Phe Ser Leu Ala Leu Val Cys Leu Glu Ala Gln Ala Trp Asp
 305 310 315 320

60
 Glu Ala Arg Ile Tyr Leu Glu Glu Leu Val Glu Arg Asp Ser His Val
 325 330 335

65
 Asp Ala Ala His Phe Asn Leu Gly Arg Leu Ala Glu Glu Gln Lys Asp
 340 345 350

70
 Thr Ala Arg Ala Leu Asp Glu Tyr Ala Gln Val Gly Pro Gly Asn Asp
 355 360 365

75
 Phe Leu Pro Ala Gln Leu Arg Gln Thr Asp Val Leu Leu Lys Ala Gly

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	370		375		380														
5	Arg 385	Val	Asp	Glu	Ala	Ala	Gln	Arg	Leu	Asp	Lys 395	Ala	Arg	Ser	Glu	Gln 400			
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	Asn	Asn	Asp	Gln	Gln	Glu	Lys	Ala	Trp	Gln	Ala	Ile	Gln	Glu	Gly	Leu			
				420					425					430					
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			435					440					445						
	Ala	Glu	Lys	Arg	Asn	Asp	Leu	Ala	Gln	Met	Glu	Lys	Asp	Leu	Arg	Phe			
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	Val	Ile	Ala	Arg	Glu	Pro	Asp	Asn	Ala	Met	Ala	Leu	Asn	Ala	Leu	Gly			
	465					470					475					480			
25	Tyr	Thr	Leu	Ala	Asp	Arg	Thr	Thr	Arg	Tyr	Gly	Glu	Ala	Arg	Glu	Leu			
					485					490					495				
	Ile	Leu	Lys	Ala	His	Lys	Leu	Asn	Pro	Asp	Asp	Pro	Ala	Ile	Leu	Asp			
30				500					505					510					
	Ser	Met	Gly	Trp	Ile	Asn	Tyr	Arg	Gln	Gly	Lys	Leu	Ala	Asp	Ala	Glu			
			515					520					525						
35	Arg	Tyr	Leu	Arg	Gln	Ala	Leu	Gln	Arg	Tyr	Pro	Asp	His	Glu	Val	Ala			
		530					535					540							
	Ala	His	Leu	Gly	Glu	Val	Leu	Trp	Ala	Gln	Gly	Arg	Gln	Gly	Asp	Ala			
40						550					555					560			
	Arg	Ala	Ile	Trp	Arg	Glu	Tyr	Leu	Asp	Lys	Gln	Pro	Asp	Ser	Asp	Val			
					565					570					575				
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	<213>	Pseudomonas aeruginosa																	
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	1				5					10					15				

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Ala Ile Ile Gly Ile Leu Ala Ala Ile Ala Ile Pro Gln Tyr Gln Asn
20 25 30

5 Tyr Val Ala Arg Ser Glu Gly Ala Ser Ala Leu Ala Thr Ile Asn Pro
35 40 45

10 Leu Lys Thr Thr Val Glu Glu Ser Leu Ser Arg Gly Ile Ala Gly Ser
50 55 60

Lys Ile Lys Ile Gly Thr Thr Ala Ser Thr Ala Thr Glu Thr Tyr Val
65 70 75 80

15 Gly Val Glu Pro Asp Ala Asn Lys Leu Gly Val Ile Ala Val Ala Ile
85 90 95

20 Glu Asp Ser Gly Ala Gly Asp Ile Thr Phe Thr Phe Gln Thr Gly Thr
100 105 110

25 Ser Ser Pro Lys Asn Ala Thr Lys Val Ile Thr Leu Asn Arg Thr Ala
115 120 125

Asp Gly Val Trp Ala Cys Lys Ser Thr Gln Asp Pro Met Phe Thr Pro
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30 Lys Gly Cys Asp Asn
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<212> PRT
<213> Artificial Sequence

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polypeptide"

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50 Asp Val Cys Ser Asp Ser Asp Asn Asp Gly Val Cys Asp Asn Val Asp
20 25 30

Lys Cys Pro Asp Thr Pro Ala Asn Val Thr Val Asp Ala Asn Gly Cys
35 40 45

55 Pro Ala Val Ala Glu Val Val Arg Val Gln Leu Asp Val Lys Phe Asp
50 55 60

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Phe Asp Lys Ser Lys Val Lys Glu Asn Ser Tyr Ala Asp Ile Lys Asn
 65 70 75 80
 5 Leu Ala Asp Phe Met Lys Gln Tyr Pro Ser Thr Ser Thr Thr Val Glu
 85 90 95
 10 Gly His Thr Asp Ser Val Gly Thr Asp Ala Tyr Asn Gln Lys Leu Ser
 100 105 110
 15 Glu Arg Arg Ala Asn Ala Val Arg Asp Val Leu Val Asn Glu Tyr Gly
 115 120 125
 20 Val Glu Gly Gly Arg Val Asn Ala Val Gly Tyr Gly Glu Ser Arg Pro
 130 135 140
 25 Val Ala Asp Asn Ala Thr Ala Glu Gly Arg Ala Ile Asn Arg Arg Val
 145 150 155 160
 30 Glu Ser Ser His Ser Lys Glu Thr Glu Ala Arg Leu Thr Ala Thr Glu
 165 170 175
 35 Asp Ala Ala Ala Arg Ala Gln Ala Arg Ala Asp Glu Ala Tyr Arg Lys
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 40 Ala Asp Glu Ala Leu Gly Ala Ala Gln Lys Ala Gln Gln Thr Ala Asp
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 45 Glu Ala Asn Glu Arg Ala Leu Arg Met Leu Glu Lys Ala Ser Arg Lys
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 <213> Pseudomonas aeruginosa
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 20 25 30
 Thr Thr Gly Tyr Arg Ile Asn Ser Ala Lys Asp Asp Ala Ala Gly Leu
 35 40 45
 60 Gln Ile Ser Asn Arg Leu Ser Asn Gln Ile Ser Gly Leu Asn Val Ala
 50 55 60

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	Thr	Arg	Asn	Ala	Asn	Asp	Gly	Ile	Ser	Leu	Ala	Gln	Thr	Ala	Glu	Gly
	65					70					75					80
5	Ala	Leu	Gln	Gln	Ser	Thr	Asn	Ile	Leu	Gln	Arg	Ile	Arg	Asp	Leu	Ala
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10	Leu	Gln	Ser	Ala	Asn	Gly	Ser	Asn	Ser	Asp	Ala	Asp	Arg	Ala	Ala	Leu
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15	Gln	Lys	Glu	Val	Ala	Ala	Gln	Gln	Ala	Glu	Leu	Thr	Arg	Ile	Ser	Asp
			115					120					125			
20	Thr	Thr	Thr	Phe	Gly	Gly	Arg	Lys	Leu	Leu	Asp	Gly	Ser	Phe	Gly	Thr
		130					135					140				
25	Thr	Ser	Phe	Gln	Val	Gly	Ser	Asn	Ala	Tyr	Glu	Thr	Ile	Asp	Ile	Ser
	145					150					155					160
30	Leu	Gln	Asn	Ala	Ser	Ala	Ser	Ala	Ile	Gly	Ser	Tyr	Gln	Val	Gly	Ser
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35	Asn	Gly	Ala	Gly	Thr	Val	Ala	Ser	Val	Ala	Gly	Thr	Ala	Thr	Ala	Ser
				180					185					190		
40	Gly	Ile	Ala	Ser	Gly	Thr	Val	Asn	Leu	Val	Gly	Gly	Gly	Gln	Val	Lys
			195					200					205			
45	Asn	Ile	Ala	Ile	Ala	Ala	Gly	Asp	Ser	Ala	Lys	Ala	Ile	Ala	Glu	Lys
		210					215					220				
50	Met	Asp	Gly	Ala	Ile	Pro	Asn	Leu	Ser	Ala	Arg	Ala	Arg	Thr	Val	Phe
	225					230					235					240
55	Thr	Ala	Asp	Val	Ser	Gly	Val	Thr	Gly	Gly	Ser	Leu	Asn	Phe	Asp	Val
					245					250					255	
60	Thr	Val	Gly	Ser	Asn	Thr	Val	Ser	Leu	Ala	Gly	Val	Thr	Ser	Thr	Gln
				260					265					270		
65	Asp	Leu	Ala	Asp	Gln	Leu	Asn	Ser	Asn	Ser	Ser	Lys	Leu	Gly	Ile	Thr
			275					280					285			
70	Ala	Ser	Ile	Asn	Asp	Lys	Gly	Val	Leu	Thr	Ile	Thr	Ser	Ala	Thr	Gly
		290					295					300				
75	Glu	Asn	Val	Lys	Phe	Gly	Ala	Gln	Thr	Gly	Thr	Ala	Thr	Ala	Gly	Gln
	305					310					315					320

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Val Ala Val Lys Val Gln Gly Ser Asp Gly Lys Phe Glu Ala Ala Ala
 325 330 335

5 Lys Asn Val Val Ala Ala Gly Thr Ala Ala Thr Thr Thr Ile Val Thr
 340 345 350

10 Gly Tyr Val Gln Leu Asn Ser Pro Thr Ala Tyr Ser Val Ser Gly Thr
 355 360 365

15 Gly Thr Gln Ala Ser Gln Val Phe Gly Asn Ala Ser Ala Ala Gln Lys
 370 375 380

20 Ser Ser Val Ala Ser Val Asp Ile Ser Thr Ala Asp Gly Ala Gln Asn
 385 390 395 400

25 Ala Ile Ala Val Val Asp Asn Ala Leu Ala Ala Ile Asp Ala Gln Arg
 405 410 415

30 Ala Asp Leu Gly Ala Val Gln Asn Arg Phe Lys Asn Thr Ile Asp Asn
 420 425 430

35 Leu Thr Asn Ile Ser Glu Asn Ala Thr Asn Ala Arg Ser Arg Ile Lys
 435 440 445

40 Asp Thr Asp Phe Ala Ala Glu Thr Ala Ala Leu Ser Lys Asn Gln Val
 450 455 460

45 Leu Gln Gln Ala Gly Thr Ala Ile Leu Ala Gln Ala Asn Gln Leu Pro
 465 470 475 480

50 Gln Ala Val Leu Ser Leu Leu Arg
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 <211> 474
 <212> PRT
 <213> Pseudomonas aeruginosa

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55 Val Asn Lys Met Val Asn Leu Glu Gly Ala Ala Lys Thr Asn Gln Leu
 20 25 30

Ala Thr Leu Glu Lys Thr Thr Thr Thr Arg Leu Thr Ala Leu Gly Gln
 35 40 45

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Phe Lys Ser Ala Ile Ser Ala Phe Gln Thr Ala Leu Thr Ala Leu Asn
 50 55 60
 5 Ser Asn Ala Val Phe Met Ala Arg Thr Ala Lys Ser Ser Asn Glu Asp
 65 70 75 80
 10 Ile Leu Lys Ala Ser Ala Thr Gln Ser Ala Val Ala Gly Thr Tyr Gln
 85 90 95
 15 Ile Gln Val Asn Ser Leu Ala Thr Ser Ser Lys Ile Ala Leu Gln Ala
 100 105 110
 20 Ile Ala Asp Pro Ala Asn Ala Lys Phe Asn Ser Gly Thr Leu Asn Ile
 115 120 125
 25 Ser Val Gly Asp Thr Lys Leu Pro Ala Ile Thr Val Asp Ser Ser Asn
 130 135 140
 30 Asn Thr Leu Ala Gly Met Arg Asp Ala Ile Asn Gln Ala Gly Lys Glu
 145 150 155 160
 35 Ala Gly Val Ser Ala Thr Ile Ile Thr Asp Asn Ser Gly Ser Arg Leu
 165 170 175
 40 Val Leu Ser Ser Thr Lys Thr Gly Asp Gly Lys Asp Ile Lys Val Glu
 180 185 190
 45 Val Ser Asp Asp Gly Ser Gly Gly Asn Thr Ser Leu Ser Gln Leu Ala
 195 200 205
 50 Phe Asp Pro Ala Thr Ala Pro Lys Leu Ser Asp Gly Ala Ala Ala Gly
 210 215 220
 55 Tyr Val Thr Lys Ala Ala Asn Gly Glu Ile Thr Val Asp Gly Leu Lys
 225 230 235 240
 Arg Ser Ile Ala Ser Asn Ser Val Ser Asp Val Ile Asp Gly Val Ser
 245 250 255
 Phe Asp Val Lys Ala Val Thr Glu Ala Gly Lys Pro Ile Thr Leu Thr
 260 265 270
 Val Ser Arg Asp Asp Ala Gly Val Lys Asp Asn Val Lys Lys Phe Val
 275 280 285
 Glu Ala Tyr Asn Thr Leu Thr Lys Phe Ile Asn Glu Gln Thr Val Val
 290 295 300

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Thr Lys Val Gly Glu Asp Lys Asn Pro Val Thr Gly Ala Leu Leu Gly
 305 310 315 320
 5 Asp Ala Ser Val Arg Ala Leu Val Asn Thr Met Arg Ser Glu Leu Ile
 325 330 335
 10 Ala Ser Asn Glu Asn Gly Ser Val Arg Asn Leu Ala Ala Leu Gly Ile
 340 345 350
 15 Thr Thr Thr Lys Asp Gly Thr Leu Glu Ile Asp Glu Lys Lys Leu Asp
 355 360 365
 20 Lys Ala Ile Ser Ala Asp Phe Glu Gly Val Ala Ser Tyr Phe Thr Gly
 370 375 380
 25 Asp Thr Gly Leu Ala Lys Arg Leu Gly Asp Lys Met Lys Pro Tyr Thr
 385 390 395
 30 Asp Ala Gln Gly Ile Leu Asp Gln Arg Thr Thr Thr Leu Gln Lys Thr
 405 410 415
 35 Leu Ser Asn Val Asp Thr Gln Lys Ala Asp Leu Ala Lys Arg Leu Ala
 420 425 430
 40 Ala Leu Gln Glu Lys Leu Thr Thr Gln Phe Asn Leu Leu Ser Ala Met
 435 440 445
 45 Gln Asp Glu Met Thr Lys Arg Gln Lys Ser Ile Thr Asp Asn Leu Ala
 450 455 460
 50 Ser Leu Pro Tyr Gly Ser Gly Lys Lys Thr
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 <212> PRT
 <213> Pseudomonas aeruginosa
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 55 Leu Ala Gly Gly Ser Phe Ala Ser Ala Ala Glu Glu Ala Phe Asp Leu
 20 25 30
 60 Trp Asn Glu Cys Ala Lys Ala Cys Val Leu Asp Leu Lys Asp Gly Val
 35 40 45

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Arg Ser Ser Arg Met Ser Val Asp Pro Ala Ile Ala Asp Thr Asn Gly
 50 55 60
 5 Gln Gly Val Leu His Tyr Ser Met Val Leu Glu Gly Gly Asn Asp Ala
 65 70 75 80
 10 Leu Lys Leu Ala Ile Asp Asn Ala Leu Ser Ile Thr Ser Asp Gly Leu
 85 90 95
 15 Thr Ile Arg Leu Glu Gly Gly Val Glu Pro Asn Lys Pro Val Arg Tyr
 100 105 110
 20 Ser Tyr Thr Arg Gln Ala Arg Gly Ser Trp Ser Leu Asn Trp Leu Val
 115 120 125
 25 Pro Ile Gly His Glu Lys Pro Ser Asn Ile Lys Val Phe Ile His Glu
 130 135 140
 30 Leu Asn Ala Gly Asn Gln Leu Ser His Met Ser Pro Ile Tyr Thr Ile
 145 150 155 160
 35 Glu Met Gly Asp Glu Leu Leu Ala Lys Leu Ala Arg Asp Ala Thr Phe
 165 170 175
 40 Phe Val Arg Ala His Glu Ser Asn Glu Met Gln Pro Thr Leu Ala Ile
 180 185 190
 45 Ser His Ala Gly Val Ser Val Val Met Ala Gln Ala Gln Pro Arg Arg
 195 200 205
 50 Glu Lys Arg Trp Ser Glu Trp Ala Ser Gly Lys Val Leu Cys Leu Leu
 210 215 220
 55 Asp Pro Leu Asp Gly Val Tyr Asn Tyr Leu Ala Gln Gln Arg Cys Asn
 225 230 235 240
 60 Leu Asp Asp Thr Trp Glu Gly Lys Ile Tyr Arg Val Leu Ala Gly Asn
 245 250 255
 65 Pro Ala Lys His Asp Leu Asp Ile Lys Pro Thr Val Ile Ser His Arg
 260 265 270
 70 Leu His Phe Pro Glu Gly Gly Ser Leu Ala Ala Leu Thr Ala His Gln
 275 280 285
 75 Ala Cys His Leu Pro Leu Glu Thr Phe Thr Arg His Arg Gln Pro Arg
 290 295 300

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Gly Trp Glu Gln Leu Glu Gln Cys Gly Tyr Pro Val Gln Arg Leu Val
 305 310 315 320
 5 Ala Leu Tyr Leu Ala Ala Arg Leu Ser Trp Asn Gln Val Asp Gln Val
 325 330 335
 10 Ile Arg Asn Ala Leu Ala Ser Pro Gly Ser Gly Gly Asp Leu Gly Glu
 340 345 350
 15 Ala Ile Arg Glu Gln Pro Glu Gln Ala Arg Leu Ala Leu Thr Leu Ala
 355 360 365
 20 Ala Ala Glu Ser Glu Arg Phe Val Arg Gln Gly Thr Gly Asn Asp Glu
 370 375 380
 25 Ala Gly Ala Ala Ser Ala Asp Val Val Ser Leu Thr Cys Pro Val Ala
 385 390 395
 30 Ala Gly Glu Cys Ala Gly Pro Ala Asp Ser Gly Asp Ala Leu Leu Glu
 405 410 415
 35 Arg Asn Tyr Pro Thr Gly Ala Glu Phe Leu Gly Asp Gly Gly Asp Ile
 420 425 430
 40 Ser Phe Ser Thr Arg Gly Thr Gln Asn Trp Thr Val Glu Arg Leu Leu
 435 440 445
 45 Gln Ala His Arg Gln Leu Glu Glu Arg Gly Tyr Val Phe Val Gly Tyr
 450 455 460
 50 His Gly Thr Phe Leu Glu Ala Ala Gln Ser Ile Val Phe Gly Gly Val
 465 470 475 480
 55 Arg Ala Arg Ser Gln Asp Leu Asp Ala Ile Trp Arg Gly Phe Tyr Ile
 485 490 495
 60 Ala Gly Asp Pro Ala Leu Ala Tyr Gly Tyr Ala Gln Asp Gln Glu Pro
 500 505 510
 65 Asp Ala Arg Gly Arg Ile Arg Asn Gly Ala Leu Leu Arg Val Tyr Val
 515 520 525
 70 Pro Arg Ser Ser Leu Pro Gly Phe Tyr Arg Thr Gly Leu Thr Leu Ala
 530 535 540
 75 Ala Pro Glu Ala Ala Gly Glu Val Glu Arg Leu Ile Gly His Pro Leu

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545 550 555 560

5 Pro Leu Arg Leu Asp Ala Ile Thr Gly Pro Glu Glu Glu Gly Gly Arg
 565 570 575

10 Leu Glu Thr Ile Leu Gly Trp Pro Leu Ala Glu Arg Thr Val Val Ile
 580 585 590

15 Pro Ser Ala Ile Pro Thr Asp Pro Arg Asn Val Gly Gly Asp Leu Asp
 595 600 605

20 Pro Ser Ser Ile Pro Asp Lys Glu Gln Ala Ile Ser Ala Leu Pro Asp
 610 615 620

 Tyr Ala Ser Gln Pro Gly Lys Pro Pro Arg Glu Asp Leu Lys
 625 630 635

25 <210> 36
 <211> 625
 <212> PRT
 <213> Pseudomonas aeruginosa

30 <400> 36
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40 Lys Leu Met Gln Ser Arg Leu Gly Phe Gly Tyr Gln Thr Ser Arg Gln
 35 40 45

45 Asp Phe Thr Trp Ala Gly Asn Arg Ser Ser Gln Asn Val Ile Ala Ser
 50 55 60

50 Ala Pro Gly Ser Ser Gly Lys Phe Leu Val Leu Gly Ala His Tyr Asp
 65 70 75 80

55 Thr Tyr Tyr Gly Arg Pro Thr Leu Gln Gly Leu Asp Asp Asn Ala Ser
 85 90 95

 Gly Ala Ala Val Leu Thr Glu Ile Ala Arg Asn Leu Gly Gly Ile Ala
 100 105 110

 Leu Glu Asn Gly Leu Glu Val Val Gly Phe Gly Ala Glu Glu Glu Gly
 115 120 125

 Leu Arg Gly Ser Arg Ala Tyr Val Glu Ser Leu Asp Ala Ser Gln Arg
 130 135 140

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Ala Asn Leu Leu Gly Met Ile Asn Leu Asp Ser Leu Val Thr Gly Asp
 145 150 155 160

5 Lys Met Tyr Ala His Ala Gly Ser Asn Ser Val Ser Asn Pro Ala Leu
 165 170 175

10 Gly Ala Tyr Arg Glu Gln Ile Leu Arg Ile Ala Arg Glu Leu Asp Ile
 180 185 190

15 Pro Leu Phe Thr Asn Pro Gly Leu Asn Ala Glu Tyr Pro Ala Gly Thr
 195 200 205

20 Gly Cys Cys Ser Asp Gly Glu Ser Phe Asn Gly Met Asp Ile Pro Val
 210 215 220

25 Leu Phe Ile Glu Ala Thr Asn Trp Glu Leu Gly Asp Leu Asp Gly Tyr
 225 230 235 240

30 Glu Gln Thr Asp Asn Pro Ala Ile Pro Gly Gly Ser Thr Trp His Asp
 245 250 255

35 Pro Ala Glu Asp Asn Lys Glu Val Leu Thr Asn Ala Leu Gly Gln Glu
 260 265 270

40 Arg Ile Glu Gln Arg Met Arg Asp Phe Ser Arg Leu Leu Thr Arg Leu
 275 280 285

45 Val Leu Glu Gln Thr Asn Ala Asp Leu Leu Ala Ser Thr Ala Ser Gly
 290 295 300

50 Gly Ala Leu Ala Arg Gln Met Glu Asp Gln Leu Gln Arg Gln His Gln
 305 310 315 320

55 Ala Leu Thr Arg Leu His Asp Arg Arg Trp Leu Thr Leu Leu Gly Ser
 325 330 335

Asn Arg Pro Val Gly Ser Phe Asp Gly Glu Val Gly Ala Glu Gly Glu
 340 345 350

Val Ser Pro Asp Ser Gly Phe Asp Met Pro Gly Asn Pro Glu Ser Arg
 355 360 365

Arg Ala Gly Val His Leu Leu Gly Asp Tyr Arg Tyr Ser Glu Ala Leu
 370 375 380

Thr Leu Gly Gly Ser Leu Ala Phe Gln Arg Ser Arg Asp Lys Leu Asp

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	Leu	Tyr	Asn	Asp 420	Gly	Gly	Pro	Glu	Trp 425	Leu	Ala	Gly	Glu	Leu	Asn	Leu
10	Gly	His	Thr	Arg	Tyr	Asp	Ser	Lys	Arg	Ser	Val	Tyr	Leu	Gln	Ala	Ala
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15	Gly	Gly	Pro	Val	Leu	Leu	Asp 455	Gln	Arg	Leu	Ser	Gly	Asp	Thr	Ser	Ala
			450									460				
20	Trp	Ser	Trp	Gly	Ala	Arg	Leu	Glu	Gly	Gly	Tyr	Asp	Phe	Ser	Phe	Gly 480
	465					470					475					
25	Glu	Leu	Arg	Ser	Gly 485	Pro	Leu	Ala	Gly	Leu	Asp	Tyr	Met	His	Tyr	Arg 495
										490						
30	Ile	Asp	Asp	Phe	Arg	Glu	Asp	Glu	Ala	Leu	Arg	Thr	Ala	Leu	Gly	Tyr
				500					505					510		
35	Glu	Lys	Gln	Asp	Tyr	Asp	Ser	Leu	Glu	Ala	Ser	Leu	Gly	Trp	Arg	Leu
			515					520					525			
40	Arg	Gly	Glu	Leu	Ala	Leu	Gly	Ala	Arg	Met	Arg	Leu	Gln	Pro	Tyr	Ala
	530						535					540				
45	Ser	Leu	Arg	Trp	Val	Arg	Glu	Leu	Ala	Asp	Gly	Arg	Leu	Asp	Asp	Met 560
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50	Asp	Leu	Thr	Ser	Arg	Gly	Asp	Gly	Arg	Val	Arg	Val	Ala	Asp	Met	Gly
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55	Gly	Val	Asp	Lys	Asp	Phe	Gly	Arg	Ala	Gln	Leu	Gly	Ala	Gln	Leu	Ala
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60	Ile	Thr	Glu	Gln	Leu	Gly	Val	Phe	Ala	Glu	Ala	Asn	Ser	Arg	Phe	Ala
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65	His	Ser	Glu	Gly	Asn	Gln	Ala	Gly	Tyr	Ser	Leu	Gly	Val	Asn	Trp	Gln
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 <211> 178
 <212> PRT
 <213> Pseudomonas aeruginosa

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15
 Lys Val Ile Asp Asn Thr Gly Thr Trp Gly Ile Arg Ala Gly Gln Gln
 35 40 45

20
 Phe Glu Gln Gly Arg Tyr Tyr Ala Thr Tyr Glu Asn Ile Ser Asp Thr
 50 55 60

25
 Ser Ser Gly Asn Lys Leu Arg Gln Gln Asn Leu Leu Gly Ser Tyr Asp
 65 70 75 80

30
 Ala Phe Leu Pro Ile Gly Asp Asn Asn Thr Lys Leu Phe Gly Gly Ala
 85 90 95

35
 Thr Leu Gly Leu Val Lys Leu Glu Gln Asp Gly Lys Gly Phe Lys Arg
 100 105 110

40
 Asp Ser Asp Val Gly Tyr Ala Ala Gly Leu Gln Ala Gly Ile Leu Gln
 115 120 125

45
 Glu Leu Ser Lys Asn Ala Ser Ile Glu Gly Gly Tyr Arg Tyr Leu Arg
 130 135 140

50
 Thr Asn Ala Ser Thr Glu Met Thr Pro His Gly Gly Asn Lys Leu Gly
 145 150 155 160

55
 Ser Leu Asp Leu His Ser Ser Ser Gln Phe Tyr Leu Gly Ala Asn Tyr
 165 170 175

Lys Phe

<210> 38
 <211> 622
 <212> PRT
 <213> Pseudomonas aeruginosa

<400> 38
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 5 Arg Phe Thr Asn Arg Val Gly Pro Thr Tyr Gln Asn Gly Ser Gly Glu
 35 40 45
 10 Ile Phe Gly Pro Thr Ala Pro Met Leu Leu Gly Asn Gln Leu Gly Ile
 50 55 60
 15 Ala Pro Gly Asp Leu Ala Ala Ser Thr Ser Pro Val Asn Ala Gln Gln
 65 70 75 80
 20 Gly Ile Ala Asp Gly Asn Asn Trp Ala Val Gly Gly Tyr Arg Thr Asp
 85 90 95
 25 Gln Ile Tyr Asp Ser Ile Thr Ala Ala Asn Gly Ser Leu Ile Glu Arg
 100 105 110
 30 Asp Asn Thr Leu Leu Arg Ser Arg Asp Gly Tyr Leu Val Asp Arg Ala
 115 120 125
 35 Arg Gln Gly Leu Gly Ala Asp Pro Asn Ala Leu Tyr Tyr Ile Thr Gly
 130 135 140
 40 Gly Gly Asn Asp Phe Leu Gln Gly Arg Ile Leu Asn Asp Val Gln Ala
 145 150 155 160
 45 Gln Gln Ala Ala Gly Arg Leu Val Asp Ser Val Gln Ala Leu Gln Gln
 165 170 175
 50 Ala Gly Ala Arg Tyr Ile Val Val Trp Leu Leu Pro Asp Leu Gly Leu
 180 185 190
 55 Thr Pro Ala Thr Phe Gly Gly Pro Leu Gln Pro Phe Ala Ser Gln Leu
 195 200 205
 60 Ser Gly Thr Phe Asn Ala Glu Leu Thr Ala Gln Leu Ser Gln Ala Gly
 210 215 220
 65 Ala Asn Val Ile Pro Leu Asn Ile Pro Leu Leu Leu Lys Glu Gly Met
 225 230 235 240
 70 Ala Asn Pro Ala Ser Phe Gly Leu Ala Ala Asp Gln Asn Leu Ile Gly
 245 250 255
 75 Thr Cys Phe Ser Gly Asn Gly Cys Thr Met Asn Pro Thr Tyr Gly Ile
 260 265 270

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Asn Gly Ser Thr Pro Asp Pro Ser Lys Leu Leu Phe Asn Asp Ser Val
 275 280 285

5 His Pro Thr Ile Thr Gly Gln Arg Leu Ile Ala Asp Tyr Thr Tyr Ser
 290 295 300

10 Leu Leu Ser Ala Pro Trp Glu Leu Thr Leu Leu Pro Glu Met Ala His
 305 310 315 320

15 Gly Thr Leu Arg Ala Tyr Gln Asp Glu Leu Arg Ser Gln Trp Gln Ala
 325 330 335

20 Asp Trp Glu Asn Trp Gln Asn Val Gly Gln Trp Arg Gly Phe Val Gly
 340 345 350

25 Gly Gly Gly Gln Arg Leu Asp Phe Asp Ser Gln Asp Ser Ala Ala Ser
 355 360 365

30 Gly Asp Gly Asn Gly Tyr Asn Leu Thr Leu Gly Gly Ser Tyr Arg Ile
 370 375 380

35 Asp Glu Ala Trp Arg Ala Gly Val Ala Ala Gly Phe Tyr Arg Gln Lys
 385 390 395 400

40 Leu Glu Ala Gly Ala Lys Asp Ser Asp Tyr Arg Met Asn Ser Tyr Met
 405 410 415

45 Ala Ser Ala Phe Val Gln Tyr Gln Glu Asn Arg Trp Trp Ala Asp Ala
 420 425 430

50 Ala Leu Thr Gly Gly Tyr Leu Asp Tyr Asp Asp Leu Lys Arg Lys Phe
 435 440 445

55 Ala Leu Gly Gly Gly Glu Arg Ser Glu Lys Gly Asp Thr Asn Gly His
 450 455 460

60 Leu Trp Ala Phe Ser Ala Arg Leu Gly Tyr Asp Ile Ala Gln Gln Ala
 465 470 475 480

65 Asp Ser Pro Trp His Leu Ser Pro Phe Val Ser Ala Asp Tyr Ala Arg
 485 490 495

70 Val Glu Val Asp Gly Tyr Ser Glu Lys Gly Ala Ser Ala Thr Ala Leu
 500 505 510

75 Asp Tyr Asp Asp Gln Lys Arg Ser Ser Lys Arg Leu Gly Ala Gly Leu

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5	Gln	Gly	Lys	Tyr	Ala	Phe	Gly	Ser	Asp	Thr	Gln	Leu	Phe	Ala	Glu	Tyr	
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50	Gly	Arg	Gln	Tyr	Arg	Ala	Leu	Gly	Arg	Ala	Ala	Leu	Leu	Pro	Arg	Leu	
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60	Thr	Thr	Arg	Gly	Asp	Phe	Lys	Glu	Asp	Arg	Asp	Tyr	Asp	Ser	Tyr	Val	
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65	Ser	Thr	Leu	Ser	Leu	Gln	Gln	Pro	Leu	Phe	Asp	Tyr	Glu	Ala	Phe	Ser	
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70	Arg	Tyr	Arg	Lys	Gly	Val	Ala	Gln	Ala	Leu	Leu	Ser	Asp	Glu	Arg	Phe	
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75	Arg	Ser	Gln	Ser	Gln	Glu	Leu	Leu	Val	Arg	Val	Leu	Glu	Ala	Tyr	Thr	
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Gly Ala Leu Leu Ala Gln Asp Gln Ile Glu Leu Ala Arg Ala Gln Lys
 130 135 140

5
 Arg Ser Tyr Arg Glu Gln Phe Gln Leu Asn Gln Arg Gln Phe Glu Arg
 145 150 155 160

10
 Gly Asn Gly Thr Arg Thr Asp Thr Leu Glu Thr Gln Ala Arg Phe Asn
 165 170 175

15
 Leu Ala Gln Ala Gln Glu Ile Glu Ala Arg Asp Ser Gln Asp Ala Ala
 180 185 190

20
 Leu Arg Glu Leu Glu Arg Leu Val Gly Ala Pro Leu Glu Ile Ala Asp
 195 200 205

25
 Leu Ala Pro Leu Gly Glu Arg Phe Gln Val Arg Pro Leu Ser Pro Ala
 210 215 220

30
 Ser Tyr Thr Ala Trp Arg Asp Leu Ala Leu Ala Glu Asn Pro Glu Leu
 225 230 235 240

35
 Ala Ser Leu Arg His Ala Val Asp Val Ala Arg Tyr Glu Val Glu Gln
 245 250 255

40
 Asn Arg Ala Asp Phe Leu Pro Arg Leu Gly Leu Tyr Ala Ser Thr Gly
 260 265 270

45
 Lys Ser Lys Ser Gly Ser Glu Asn Thr Tyr Asn Gln Arg Tyr Glu Thr
 275 280 285

50
 Asp Ser Val Gly Ile Gln Leu Ser Val Pro Leu Phe Ser Gly Gly Glu
 290 295 300

55
 Thr Leu Ala Ala Thr Arg Gln Ala Thr His Arg Met Glu Lys Ser His
 305 310 315 320

60
 Tyr Asp Leu Asp Asp Lys Val Arg Glu Thr Leu Asn Gln Val Arg Lys
 325 330 335

65
 Met Tyr Asn Gln Ser Ser Ser Ser Ala Ala Lys Ile Arg Ala Tyr Glu
 340 345 350

70
 Met Thr Val Asp Ser Ala Arg Thr Leu Val Met Ala Thr Arg Lys Ser
 355 360 365

75
 Ile Ala Ala Gly Val Arg Val Asn Leu Asp Leu Leu Asn Ala Glu Gln

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370 375 380

5 Ala Leu Tyr Ser Ala Met Asn Glu Leu Ser Lys Ala Lys Tyr Asp Tyr
385 390 395 400

10 Leu Thr Ala Trp Ala Arg Leu Arg Phe Tyr Ala Gly Val Leu Asp Glu
405 410 415

15 Ala Asp Leu Glu Leu Val Ala Ala Asn Phe Val Ser Gly Glu Thr Pro
420 425 430

20 Ala Arg Arg Arg Asp Cys Ala Thr Thr Asp Cys Pro Ala Pro Leu His
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25 Thr Leu Ser Lys Thr Asp Thr Glu Glu Asn Arg Ser Ala Leu Asn
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<212> PRT
<213> Pseudomonas aeruginosa

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35 Ser Tyr Val Ser Asn Ile Val Gly Asp Lys Ala Glu Val Val Pro Leu
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40 Ile Pro Ala Gly Phe Asn Pro His Ala Tyr Glu Pro Arg Ala Glu Asp
35 40 45

45 Ile Lys Arg Ile Gly Thr Leu Asp Val Val Val Leu Asn Gly Val Gly
50 55 60

50 His Asp Asp Phe Ala Glu Arg Met Ile Ala Ser Ser Glu Lys Pro Gly
65 70 75 80

55 Ile Pro Val Ile Glu Ala Asn Ala Lys Val Pro Leu Leu Ala Ala Thr
85 90 95

60 Gly Met Ala Ala Arg Gly Ala Gly Lys Val Val Asn Pro His Thr Phe
100 105 110

65 Leu Ser Ile Ser Ala Ser Ile Thr Gln Val Asn Thr Ile Ala Arg Glu
115 120 125

70 Leu Gly Lys Leu Asp Pro Ala Asn Ala Lys Ala Tyr Thr Arg Asn Ala
130 135 140

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Arg Ala Tyr Ala Lys Arg Leu Arg Ala Leu Arg Ala Asp Ala Leu Ala
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5 Arg Leu Asn Lys Ala Pro Ala Ala Asp Phe Arg Val Ala Thr Ile His
 165 170 175

10 Gly Ala Tyr Asp Tyr Leu Leu Arg Glu Phe Gly Leu Glu Val Thr Ala
 180 185 190

15 Val Val Glu Pro Ala His Gly Ile Glu Pro Ser Pro Ser Gln Leu Lys
 195 200 205

Lys Thr Ile Asp Gln Leu Lys Ala Leu Asp Val Lys Val Ile Phe Ser
 210 215 220

20 Glu Ile Asp Phe Pro Ser Thr Tyr Val Glu Thr Ile Gln Arg Glu Ser
 225 230 235 240

25 Gly Val Lys Leu Tyr Ser Leu Ser His Ile Ser Tyr Gly Asp Tyr Ser
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30 Ala Gly Lys Tyr Glu Glu Glu Met Ala Arg Asn Leu Asp Thr Val Val
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Arg Ala Ile Gln Glu Ser Gly Ala
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35 <210> 41
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 <212> PRT
 <213> Pseudomonas aeruginosa

40 <400> 41
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50 Gly Glu Phe Val Arg Arg Ala Gly Glu Gln Ala Thr Phe Arg Leu Lys
 35 40 45

Pro Glu Ala Gln Trp Leu Gly Arg Gly Ser Ala Thr Leu Leu Ala Ala
 50 55 60

55 Ala Pro Pro Trp Arg Pro Gly Gln Gly Asp Ile Asn Leu Gly Gln Val
 65 70 75 80

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Ser Ile Gly Ser Gly Glu Val Pro Phe Asn Ser Ser Gln Gln Gln Ala
 85 90 95
 5 Gly Arg Leu Leu Thr Gly Leu Leu Glu Gly Arg Ser Pro Leu Val Arg
 100 105 110
 His Arg Thr Trp Gln Gly Asp Arg Leu Glu Val Arg Leu Leu Pro Ala
 115 120 125
 10 Arg Phe Ala Ser Val Tyr Ser Gln Tyr Gln Ala Cys Ile Ala Lys Leu
 130 135 140
 15 Leu Pro Val Asn Phe Asp Gln Val Lys Leu Ala Gln Val Gly Phe Pro
 145 150 155 160
 20 Asp Gly Gly Thr Ala Leu Asn Asp Val Ala Arg Ala Lys Leu Asp Ile
 165 170 175
 Ile Leu Gln Leu Leu Lys Ala Asp Pro Ser Ile Asn Arg Ile Glu Leu
 180 185 190
 25 Asp Gly His Ser Asp Asn Ser Gly Asn Arg Leu Thr Asn Arg Asp Leu
 195 200 205
 30 Ser Arg Arg Arg Ala Leu Ala Val Gln Glu Tyr Leu Lys Ser Asn Gly
 210 215 220
 35 Val Pro Glu Ser Gln Ile Asn Val Arg Phe Tyr Gly Glu Arg Tyr Pro
 225 230 235 240
 Leu Val Ala Asn Asn Ser Ala Ala Asn Arg Ala Arg Asn Arg Arg Val
 245 250 255
 40 Thr Val His Leu Ser Arg Glu Ala Val Val Glu Pro Ala Thr Glu Ala
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 45 Pro Lys Ala Glu Asp Lys Pro Ala Pro Pro Ala Ala Glu Pro Ala Ala
 275 280 285
 50 Pro Lys Pro Pro Ala Ala Ser Leu Gln Gly Lys Pro Thr Val
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 <212> PRT
 55 <213> Pseudomonas aeruginosa
 <400> 42

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 5 His Leu Ser Gly Gly Asn Ser Leu Ser Val Asn Gln Lys Val Asp Lys
 10 Leu Ile Ala Asn Trp Asp Ser Phe Ser Val Ala Ala Gly Glu Arg Val
 15 Ile Phe Asn Gln Pro Ser Ser Ser Ser Ile Ala Leu Asn Arg Val Ile
 20 Gly Thr Lys Ala Ser Asp Ile Gln Gly Arg Ile Asp Ala Asn Gly Gln
 25 Val Phe Leu Val Asn Pro Asn Gly Val Leu Phe Gly Arg Gly Ala Gln
 30 Val Asn Val Gly Gly Leu Val Ala Ser Thr Leu Asp Ile Thr Asp Ala
 35 Glu Phe Asn Gly Asn Ser Ser Arg Tyr Arg Phe Thr Gly Pro Ser Thr
 40 Asn Gly Val Leu Asn His Gly Gly Ala Ile Thr Ala Ala Glu Gly Gly
 45 Ser Ile Ala Leu Leu Gly Ala Gln Val Asp Asn Arg Gly Thr Val Leu
 50 Ala Gln Met Gly Gly Val Gly Leu Gly Ala Gly Ser Asp Leu Thr Leu
 55 Asn Phe Asp Gly Asn Lys Leu Leu Asp Ile Arg Val Asp Ala Gly Val
 60 Ala Asn Ala Leu Ala Ser Asn Gly Gly Leu Leu Lys Ala Asp Gly Gly
 65 Arg Val Leu Met Ala Ala Arg Thr Ala Asn Ala Leu Leu Asn Thr Val
 70 Val Asn Ser Gln Gly Ala Ile Glu Ala Arg Ser Leu Arg Gly Lys Asn
 75 Gly Arg Ile Val Leu Asp Gly Gly Pro Asp Gly Lys Val Met Val Gly
 80 85 90 95 100 105 110 115 120 125 130 135 140 145 150 155 160 165 170 175 180 185 190 195 200 205 210 215 220 225 230 235 240 245 250 255

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Gly Ala Leu Ser Ala Asn Ala Leu Asn Gly Pro Gly His Gly Gly Thr
 260 265 270
 5 Val Glu Val Arg Gly Gln Ala Val Glu Val Ala Leu Gly Thr Gln Val
 275 280 285
 10 Asn Thr Leu Ala Ser Asn Gly Leu Asn Gly Thr Trp Lys Ile Ala Ala
 290 295 300
 15 Asp Lys Ile Asp Val Arg Pro Ser Ala Val Ser Asp Gly Val Thr Val
 305 310 315 320
 20 His Ala Asp Thr Leu Ser Arg Asn Leu Ala Ser Thr Asn Ile Glu Leu
 325 330 335
 25 Val Ser Thr Lys Gly Asp Leu Asp Leu Asp Gly Ser Val Asn Trp Ala
 340 345 350
 30 Ser Gly Asn Arg Leu Gly Leu Gly Ser Ala Ala Asp Leu Thr Leu Asn
 355 360 365
 35 Gly Arg Leu Asn Ala Ser Gly Ala Lys Ala Gly Leu Glu Leu Lys Ala
 370 375 380
 40 Glu Gly Ala Ile Asp Ile Asn Asp Lys Ile Val Leu Gly Gly Ala Gly
 385 390 395 400
 45 Ser Ala Leu Ala Met Asp Ala Gly Glu Gly His Arg Val Asn Gly Thr
 405 410 415
 50 Ala Ser Val Ser Leu Ala Gly Ala Asn Ala Thr Tyr Val Ser Gly Gly
 420 425 430
 55 Tyr Tyr Tyr Thr Val Val Gln Asn Leu Ala Gln Leu Gln Ala Ile Asn
 435 440 445
 60 Lys Asn Leu Asp Gly Leu Tyr Val Leu Gly Gly Asn Ile Leu Gly Gly
 450 455 460
 65 Ser Tyr Tyr Cys Thr Ala Leu Gln Ser Ile Gly Gly Pro Ala Gly Val
 465 470 475 480
 70 Phe Ser Gly Thr Leu Asp Gly Leu Gly Asn Ser Ile Gly Asn Leu Ser
 485 490 495
 75 Ile Ser Asn Thr Gly Pro Asn Val Gly Leu Phe Ala Arg Ser Ser Gly
 500 505 510

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5 Tyr Gly
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 <212> PRT
 <213> Pseudomonas aeruginosa

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25 Gln Val Arg Phe Ile Met Gly Asn Pro Leu Ile Val Asp Thr Phe His
 35 40 45

30 Ala Asn Arg Trp Asp Tyr Leu Tyr Ser Ile Gln Pro Gly Gly Gly Arg
 50 55 60

35 Arg Gln Gln Glu Arg Val Ser Leu Phe Phe Asn Asp Ser Asp Gln Leu
 65 70 75 80

40 Ala Gly Leu Asn Gly Asp Phe Met Pro Gly Val Ser Arg Asp Glu Ala
 85 90 95

45 Ile Leu Gly Lys Glu Gly Ser Thr Thr Val Thr Gln Pro Ala Asp Gln
 100 105 110

50 Gln Lys Pro Glu Ala Gln Lys Glu Glu Pro Pro Lys Pro Gly Ser Thr
 115 120 125

55 Leu Glu Gln Leu Gln Arg Glu Val Asp Glu Ala Gln Pro Val Pro Val
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Pro Thr Pro Glu Pro Leu Asp Pro Ser Pro Gln
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60 <210> 44
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 <212> PRT
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				20					25					30			
10	Lys	Gln	Phe	Pro	Arg	Tyr	Asn	Asp	Glu	Lys	Leu	Gln	Ala	Tyr	Val	Gln	
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15	Arg	Val	Gly	Glu	Arg	Val	Ala	Arg	Ser	Ser	His	Arg	Ser	Asn	Leu	Gln	
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20	Tyr	His	Phe	Thr	Val	Ile	Asp	Ser	Pro	Asp	Ile	Asn	Ala	Phe	Ala	Leu	
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25	Pro	Gly	Gly	Tyr	Ile	Tyr	Ile	His	Arg	Gly	Leu	Ile	Ala	Tyr	Leu	Gly	
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30	Ser	Glu	Ala	Glu	Leu	Ala	Ala	Val	Leu	Gly	His	Glu	Val	Gly	His	Val	
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35	Thr	Ala	Arg	His	Ser	Val	Arg	Gln	Gln	Ser	Gln	Ala	Ser	Ala	Trp	Asn	
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40	Ile	Leu	Gly	Gln	Ala	Val	Ala	Ile	Gly	Thr	Gly	Val	Gly	Ala	Ala	Gly	
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50	Asp	Met	Glu	Leu	Glu	Ala	Asp	Gly	Leu	Gly	Ala	Gln	Tyr	Leu	Ala	Arg	
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55	Ala	Gly	Tyr	Asp	Pro	Thr	Ala	Met	Ile	Gln	Val	Val	Arg	Val	Leu	Lys	
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60	Asn	Gln	Glu	Asp	Phe	Ala	Arg	Glu	Glu	Ala	Ala	Arg	Asn	Gly	Gln	Ala	
			195					200					205				
65	Val	Gln	Ala	Gly	Gly	Tyr	His	Gly	Leu	Phe	Asp	Thr	His	Pro	Asp	Asn	
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70	Asp	Arg	Arg	Leu	Gln	Glu	Val	Val	Gly	Pro	Ala	Arg	Gln	Leu	Ala	Asn	
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75	Gly	Gln	Gln	Glu	Val	Gly	Arg	Glu	Val	Phe	Leu	Arg	His	Leu	Glu	Gly	
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Met Pro Phe Gly Asp Ser Ala Ser Ala Gly Val Arg Arg Gly Gln Asn
 260 265 270

5 Phe Tyr His Ala Glu Leu Asp Phe Thr Leu Ser Tyr Pro Ala Gly Trp
 275 280 285

10 Lys Ile Leu Asn Gln Pro Ser Ala Leu Leu Gly Tyr Pro Ala Asp Glu
 290 295 300

Gln Ser Phe Ile Gly Met Lys Leu Val Pro His Asp Ser Arg Leu Thr
 305 310 315 320

15 Pro Ala Glu Phe Leu Arg Lys Asn Ala Gly Gln Arg Leu Ala Gln Glu
 325 330 335

20 Glu Ser Leu Lys Gln Ala Gly Leu Asn Gly Tyr Thr Ala Val Val Pro
 340 345 350

Gly Asn Pro Ala Arg Arg Val Ala Val Ile Tyr Gln Gly Asp Arg Ala
 355 360 365

25 Tyr Leu Phe Val Gly Val Val Lys Val Gly Ser Leu Glu Thr Gln Asp
 370 375 380

30 Asp Arg Phe Leu Ser Val Ile Arg Ser Phe Arg Pro Leu Arg Asp Lys
 385 390 395 400

Glu Arg Ala Leu Ala Gln Pro Arg Arg Leu His Leu Val Gln Val Lys
 405 410 415

35 Ala Gly Gln Thr Leu Glu Gln Leu Ala Ala Gly Gly Glu Gly Ser Leu
 420 425 430

40 Ser Asp Ser Val Ala Arg Leu Arg Leu Leu Asn Asp Leu Tyr Pro Ser
 435 440 445

45 Gly Glu Pro Arg Pro Gly Asp Trp Leu Lys Val Val Arg
 450 455 460

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 <212> PRT
 50 <213> Pseudomonas aeruginosa

<400> 45
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55 Ile Asp Ala Ala Ser Lys Asp Gly Lys Leu Arg Glu Ala Leu Leu Ala

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10	Thr	Phe	Ser	Asn	Gly	Phe	Glu	Leu	Gly	Glu	Gly	Thr	Leu	Ser	Lys	Ser			
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15	Asp	Asp	Glu	His	Trp	Lys	Val	Ala	Phe	Tyr	Gly	Asp	Asp	Asn	Gln	Glu			
	65					70					75				80				
20	Ser	Leu	Glu	Leu	Asp	Gly	Lys	Glu	Leu	Ile	Gln	Gln	Ala	Ser	Ala	Asn			
					85					90					95				
25	Gly	Pro	Glu	Gln	Arg	Phe	Arg	Arg	Leu	Asp	Pro	Gln	Pro	Ala	Ala	Ser			
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30	Ser	Pro	Ala	Gly	Ser	Gly	Phe	Glu	Arg	Ala	Leu	Tyr	Gly	Ser	Tyr	Leu			
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35	Lys	Gly	Ser	Trp	Lys	Ile	Arg	Glu	Gly	Gln	Gly	Gln	Gly	Gly	Lys	Val			
		130					135					140							
40	Glu	Phe	Gln	Ala	Asn	Gly	Leu	Val	Ser	Gly	Leu	Pro	Gly	Ala	Glu	Arg			
	145					150					155					160			
45	Tyr	Ala	Leu	Cys	Leu	Ala	Gly	Asp	Cys	Ala	Ala	Met	Ser	Gly	Asp	Asn			
				165						170					175				
50	Asp	Ser	Ile	Trp	Leu	Gln	Gln	Gly	Asn	Arg	Gly	Arg	Glu	Leu	Leu	Phe			
				180					185					190					
55	Ser	Leu	Asp	Asp	Asp	Glu	Leu	Gln	Leu	Phe	Glu	Ala	Val	Asn	Thr	Ala			
			195					200					205						
60	Gly	Ala	Asn	Glu	Met	Pro	Ser	Tyr	Val	Pro	Gly	Lys	Arg	Val	Trp	Leu			
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65	Leu	Glu	Arg																
	225																		
70	<210>	46																	
	<211>	891																	
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	1				5					10					15				

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Ser Pro Leu Gln Asn Ala Asn Ala Asn Leu Pro Pro Arg Pro Ala His
 20 25 30
 5 Thr Ala Thr Ser Val Ser Thr Ala Ala Ala Gly Ser Ser Val Ser Gly
 35 40 45
 10 Ser Gly Gly Glu Thr Val Glu Ala Glu Pro Thr Gln Arg Leu Val Thr
 50 55 60
 15 Glu Ser Gly Gly Arg Ala Leu Lys Ser Arg Ser Ala Asp Tyr Ser His
 65 70 75 80
 20 Leu Asp Trp Ile Pro Arg Glu Lys Leu Thr Ala Ala Gln Leu Ala Glu
 85 90 95
 25 Ile Gly Pro Tyr Cys Gly Gly Ser Tyr Ile Glu Pro Val Arg Pro Gly
 100 105 110
 30 Met Asp Asp Gly Ala Pro Ser Asp Glu Ser Pro Thr Tyr Val Ser Ala
 115 120 125
 35 Lys Ala Ser Arg Tyr Glu Gln Glu Lys Gln Ile Ala Thr Leu Ala Gly
 130 135 140
 40 Asp Val Val Leu Arg Gln Gly Ser Met Gln Val Glu Gly Asp Glu Ala
 145 150 155 160
 45 Asn Leu His Gln Leu Glu Asn Arg Gly Glu Leu Val Gly Asn Val Lys
 165 170 175
 50 Leu Arg Asp Lys Gly Met Leu Val Val Gly Asp His Ala Gln Val Gln
 180 185 190
 55 Leu Asp Asn Gly Glu Ala Gln Val Asp Asn Ala Glu Tyr Val Ile His
 195 200 205
 60 Lys Ala His Ala Arg Gly Ser Ala Leu Tyr Ala Lys Arg Ser Glu Asn
 210 215 220
 65 Ala Ile Ile Met Leu Lys Asp Gly Thr Tyr Thr Arg Cys Glu Pro Ser
 225 230 235 240
 70 Ser Asn Ala Trp Thr Leu Lys Gly Asn Asn Val Lys Leu Asn Pro Ala
 245 250 255
 75 Thr Gly Phe Gly Thr Ala Thr Asn Ala Thr Leu Arg Val Lys Asp Phe

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	260					265					270					
5	Pro	Val	Phe	Tyr	Thr	Pro	Tyr	Ile	Tyr	Phe	Pro	Ile	Asp	Asp	Arg	Arg
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10	Gln	Ser	Gly	Phe	Leu	Pro	Pro	Ser	Phe	Ser	Ser	Thr	Ser	Asp	Thr	Gly
		290					295					300				
15	Phe	Thr	Leu	Val	Thr	Pro	Tyr	Tyr	Phe	Asn	Leu	Ala	Pro	Asn	Tyr	Asp
	305					310					315					320
20	Ala	Thr	Leu	Tyr	Pro	Arg	Tyr	Met	Ala	Lys	Arg	Gly	Met	Met	Leu	Glu
					325					330					335	
25	Gly	Glu	Phe	Arg	Tyr	Leu	Thr	His	Ser	Ser	Glu	Gly	Ile	Val	Asn	Ala
				340					345					350		
30	Ala	Tyr	Leu	Asn	Asp	Lys	Asp	Asp	His	Arg	Glu	Gly	Phe	Pro	Asp	Tyr
			355					360					365			
35	Ser	Lys	Asp	Arg	Trp	Leu	Tyr	Gly	Leu	Lys	Asn	Thr	Thr	Gly	Leu	Asp
		370					375					380				
40	Ser	Arg	Trp	Leu	Ala	Glu	Val	Asp	Tyr	Thr	Arg	Ile	Ser	Asp	Pro	Tyr
	385					390					395					400
45	Tyr	Phe	Gln	Asp	Leu	Asp	Thr	Asp	Leu	Gly	Val	Gly	Ser	Thr	Thr	Tyr
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50	Val	Asn	Gln	Arg	Gly	Thr	Leu	Thr	Tyr	Arg	Gly	Asp	Thr	Phe	Thr	Gly
				420					425					430		
55	Arg	Leu	Asn	Ala	Gln	Ala	Tyr	Gln	Leu	Ala	Thr	Thr	Thr	Asp	Val	Thr
			435					440					445			
60	Pro	Tyr	Asp	Arg	Leu	Pro	Gln	Ile	Thr	Phe	Asp	Gly	Phe	Leu	Pro	Tyr
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65	Asn	Pro	Gly	Gly	Met	Gln	Phe	Thr	Tyr	Gly	Thr	Glu	Phe	Val	Arg	Phe
	465					470					475					480
70	Asp	Arg	Asp	Leu	Asp	Glu	Asn	Ile	Tyr	Phe	Asn	Asp	Asp	Gly	Ser	Ile
					485					490					495	
75	Arg	Gly	Lys	Arg	Pro	Asp	Ala	Ser	Leu	Gln	Gly	Leu	Ala	Arg	Ala	Thr
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Gly Asp Arg Met His Leu Glu Pro Gly Met Ser Leu Pro Met Thr Arg
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5 Ser Trp Gly Tyr Val Thr Pro Thr Leu Lys Tyr Leu Tyr Thr Lys Tyr
 530 535 540

10 Asp Leu Asp Leu Asp Ser Gln Gly Lys Thr Asp Leu Asn Lys Arg Asp
 545 550 555 560

15 Glu Ser Phe Asp Ser Asn Gln Asp Arg Ser Leu Pro Leu Val Lys Val
 565 570 575

20 Asp Ser Gly Leu Tyr Phe Asp Arg Asp Thr Thr Phe Ala Gly Thr Pro
 580 585 590

25 Phe Arg Gln Thr Leu Glu Pro Arg Ala Met Tyr Leu Tyr Val Pro Tyr
 595 600 605

30 Lys Asp Gln Asp Ser Leu Pro Val Phe Asp Thr Ser Glu Pro Ser Phe
 610 615 620

35 Ser Tyr Asp Ser Leu Trp Arg Glu Asn Arg Phe Thr Gly Lys Asp Arg
 625 630 635 640

40 Ile Gly Asp Ala Asn Gln Leu Ser Leu Gly Val Thr Ser Arg Phe Ile
 645 650 655

45 Glu Glu Asn Gly Phe Glu Arg Ala Ser Ile Ser Ala Gly Gln Ile Tyr
 660 665 670

50 Tyr Phe Arg Asp Arg Arg Val Gln Leu Pro Gly Leu Thr Glu Lys Asp
 675 680 685

55 Leu Lys Arg Leu Asn Leu Asp Pro Ser Gly Leu Asp Asn Asp Ser Trp
 690 695 700

60 Arg Ser Pro Tyr Ala Phe Ala Gly Gln Tyr Arg Phe Asn Arg Asp Trp
 705 710 715 720

65 Arg Ile Asn Ser Asp Phe Asn Trp Asn Pro Asn Thr Ser Arg Thr Glu
 725 730 735

70 Ser Gly Ser Ala Ile Phe His Tyr Gln Pro Glu Val Asp Pro Gly Lys
 740 745 750

75 Val Val Asn Val Gly Tyr Arg Tyr Arg Ala Asp Ala Arg Arg Phe Asp
 755 760 765

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Ser Ser Arg Gly Thr Phe Arg Tyr Gly Asn Glu Asn Asp Ile Ile Lys
770 775 780

5 Gln His Asp Phe Ser Val Ile Trp Pro Leu Val Pro Gln Trp Ser Val
785 790 795 800

10 Leu Ala Arg Trp Gln Tyr Asp Tyr Asn Lys Asn Arg Thr Leu Glu Ala
805 810 815

15 Phe Gly Gly Phe Glu Tyr Asp Ser Cys Cys Trp Lys Leu Arg Leu Ile
820 825 830

20 Asn Arg Tyr Trp Leu Asp Val Asp Asp Ala Phe Leu Val Gln Ser
835 840 845

25 Glu Lys Ala Asp Arg Gly Ile Phe Leu Gln Ile Val Leu Lys Gly Leu
850 855 860

30 Gly Gly Ile Val Gly Asn Lys Thr Glu Met Phe Leu Asp Lys Gly Ile
865 870 875 880

Gln Gly Tyr Arg Gln Arg Glu Asp Gln Ala Met
885 890

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<212> PRT
<213> Pseudomonas aeruginosa

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1 5 10 15

40 Asn Lys Gly Gly Ala Thr Ala Leu Val Val Asp Thr Gln Gln Asn Tyr
20 25 30

45 Asn Asn Lys Val Ser Asn Phe Gly Thr Leu Asn Asn Ala Ser Val Ser
35 40 45

50 Gly Ser Ile Lys Asp Ala Ser Gly Asn Val Gly Val Asn Val Ala Ala
50 55 60

55 Gly Asp Asn Asn Gln Gln Ala Asn Ala Ala Leu Ala Ser Ala Asp
65 70 75 80

Ala Ser Phe Val Phe Gly Thr Ala Thr Ala Ser Thr Ser Val Leu Gln
85 90 95

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Ser Gly Tyr Gly Asn Thr Leu Asn Asn Tyr Ser Asn Pro Asn Thr Ala
 100 105 110
 5 Ser Leu Ser Asn Ser Ala Asn Asn Val Ser Gly Asn Leu Gly Val Asn
 115 120 125
 Val Ala Ala Gly Asn Phe Asn Gln Gln Lys Asn Asp Leu Ala Ala Ala
 10 130 135 140
 Val Ser Asn Gly Gln Tyr Ser Thr Ala Gly Ser Ala Ala Ser Gln Thr
 145 150 155 160
 15 Ser Thr Gly Asn Thr Thr Val Asn Ser Ala Asn Tyr Ala Tyr Gly Gly
 165 170 175
 Thr Tyr Val Ser Leu Lys Leu Asn Ala Asp Gly Ser Tyr Lys Gly Thr
 20 180 185 190
 Ser Asp Gln Ile Gly Asp Val Tyr Leu Asp Thr Trp Glu Gly Gln Thr
 25 195 200 205
 His Pro Gly Gly Ser Asn Thr Gly His Ile Asp Val Asp Ser Gln Ala
 210 215 220
 30 Gln Gly Ala Lys Asp Leu Asn His Asp Gly Gly Ala Phe Ala Phe Lys
 225 230 235 240
 Glu Lys Gly Asp Val Asp Leu Lys Gly Thr Val Ser Gly Phe Ile Pro
 35 245 250 255
 Ala Ile Val Gly Phe Lys Thr Pro Val Thr Asn Asn Ala Ser Leu Ser
 260 265 270
 40 Asn Ser Leu Gln Asn Val Ser Gly Asn Val Gly Val Asn Ile Ala Ala
 275 280 285
 Gly Gly Gly Asn Gln Gln Ser Asn Ser Leu Ser Ile Ala Ala Gly Cys
 45 290 295 300
 Ser Ser Cys Pro Ala Gly Gly Glu Ser Leu Gly Phe
 305 310 315
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 <211> 242
 <212> PRT
 <213> Pseudomonas aeruginosa
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 Cys Ser Thr Pro Pro Asn Ala Asn Leu Glu Gln Ala Arg Ser Asn Phe

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			20					25					30			
10	Thr	Lys	Asp	Ala	Gly	Asp	Trp	Leu	Ala	Lys	Ala	Asp	Lys	Ala	Tyr	Gln
			35					40					45			
15	Asp	Gly	Glu	Asp	Gln	Arg	Asp	Val	Asp	Gln	Leu	Ala	Tyr	Leu	Thr	Asn
		50					55					60				
20	Gln	Arg	Ile	Glu	Leu	Ala	Lys	Gln	Thr	Ile	Val	Leu	Arg	Asn	Ala	Glu
	65					70					75					80
25	Ala	Gln	Leu	Gln	Asn	Ala	Ser	Ala	Gln	Arg	Ala	Gln	Ala	Arg	Leu	Asp
				85						90					95	
30	Ala	Arg	Thr	Ala	Gln	Leu	Asp	Lys	Leu	Arg	Ser	Gln	Leu	Asn	Ala	Lys
			100						105					110		
35	Gln	Thr	Ser	Arg	Gly	Thr	Met	Val	Thr	Phe	Gly	Asp	Val	Leu	Phe	Asp
			115					120					125			
40	Leu	Asp	Lys	Ser	Asp	Leu	Lys	Pro	Gly	Ala	Met	Arg	Asn	Ile	Gln	Gln
		130					135					140				
45	Leu	Ala	Glu	Phe	Leu	Gln	Gln	Asn	Pro	Glu	Arg	Gln	Val	Ile	Val	Glu
	145					150					155					160
50	Gly	Tyr	Thr	Asp	Ser	Thr	Gly	Ser	Ala	Asn	Tyr	Asn	Gln	Arg	Leu	Ser
				165						170					175	
55	Glu	Arg	Arg	Ala	Asp	Ser	Val	Arg	Met	Ala	Leu	Leu	Ser	Arg	Gly	Ile
			180						185					190		
60	Ser	Pro	Glu	Arg	Val	Ala	Thr	Arg	Gly	Tyr	Gly	Lys	Glu	Tyr	Pro	Val
			195					200					205			
65	Ala	Ser	Asn	Gly	Thr	Ser	Ser	Gly	Arg	Ala	Met	Asn	Arg	Arg	Val	Glu
		210					215					220				
70	Val	Thr	Ile	Ser	Asn	Asp	Ala	Lys	Pro	Val	Ala	Pro	Arg	Ser	Ser	Val
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75	Ser	Gly														

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 <211> 426
 <212> PRT
 <213> Pseudomonas aeruginosa

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15
 Ala Ala Ala Lys Ala Val Ile Lys Asn Tyr Ala Asp Leu Ala Glu Ala
 35 40 45

20
 Thr Phe Ala Asp Ala Leu Ser Thr Ala Lys Asp Leu Gln Lys Ala Ile
 50 55 60

25
 Asp Ala Phe Leu Ala Lys Pro Asp Ala Glu Thr Leu Lys Ala Ala Lys
 65 70 75 80

30
 Glu Ala Trp Phe Ala Ala Arg Thr Pro Tyr Ser Gln Ser Glu Ala Phe
 85 90 95

35
 Arg Phe Gly Asn Ala Ile Ile Asp Asp Trp Glu Gly Gln Val Asn Ala
 100 105 110

40
 Trp Pro Leu Asp Glu Gly Leu Ile Asp Tyr Val Ala Lys Asp Tyr Gln
 115 120 125

45
 His Ala Leu Gly Asn Pro Gly Ala Thr Ala Asn Ile Val Ala Asn Thr
 130 135 140

50
 Glu Ile Gln Val Gly Glu Asp Lys Ile Asp Val Lys Glu Ile Thr Gly
 145 150 155 160

55
 Glu Lys Leu Ala Ser Leu Asn Glu Leu Gly Gly Ser Glu Ala Asn Val
 165 170 175

Ala Thr Gly Tyr His Ala Ile Glu Phe Leu Leu Trp Gly Gln Asp Leu
 180 185 190

Asn Gly Thr Gly Pro Gly Ala Gly Asn Arg Pro Ala Thr Asp Tyr Ala
 195 200 205

Gln Gly Lys Asp Cys Thr Gly Gly His Cys Asp Arg Arg Ala Ala Tyr
 210 215 220

Leu Lys Ala Val Thr Asp Leu Leu Val Ser Asp Leu Glu Tyr Met Ala

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	225					230					235					240
5	Gly	Gln	Trp	Lys	Ala	Gly	Val	Ala	Asp	Asn	Tyr	Arg	Ala	Lys	Leu	Glu
					245					250					255	
10	Ala	Glu	Pro	Val	Asp	Thr	Gly	Leu	Arg	Lys	Met	Phe	Phe	Gly	Met	Gly
				260					265					270		
15	Ser	Leu	Ser	Leu	Gly	Glu	Leu	Ala	Gly	Glu	Arg	Met	Lys	Val	Ala	Leu
			275					280					285			
20	Glu	Ala	Asn	Ser	Thr	Glu	Asp	Glu	His	Asp	Cys	Phe	Ser	Asp	Asp	Thr
		290					295					300				
25	His	His	Thr	Leu	Phe	Phe	Asn	Gly	Lys	Ser	Ile	Arg	Asn	Ile	Tyr	Leu
	305					310					315					320
30	Gly	Glu	Tyr	Lys	Arg	Ile	Asp	Gly	Ser	Val	Val	Lys	Gly	Pro	Ser	Leu
					325					330					335	
35	Ala	Asp	Leu	Val	Ala	Lys	Ala	Asp	Ala	Ala	Ala	Asn	Asp	Thr	Leu	Lys
				340					345					350		
40	Ala	Asp	Leu	Ala	Asp	Thr	Glu	Ala	Lys	Leu	Gln	Ala	Ile	Val	Asp	Ser
			355					360					365			
45	Ala	Glu	Lys	Asp	Gly	Val	His	Phe	Asp	Gln	Met	Ile	Ala	Pro	Asp	Asn
	370						375					380				
50	Lys	Asp	Gly	Gln	Gln	Lys	Ile	Arg	Asp	Ala	Ile	Ala	Ala	Leu	Val	Lys
	385					390					395					400
55	Gln	Thr	Gly	Ala	Ile	Glu	Gln	Ala	Ala	Gly	Lys	Leu	Gly	Ile	Gln	Asp
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	Leu	Lys	Pro	Asp	Asn	Ala	Asp	His	Glu	Phe						
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	<212> PRT															
	<213> Pseudomonas aeruginosa															
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	Glu	Gln	Ala	Val	Asp	Ser	Val	Pro	Ser	Thr	Val	Ser	Val	Gln	Thr	Arg
				20					25					30		

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Glu Gln Leu Asp Arg Gln Asn Val Asn Asn Ile Lys Glu Leu Val Arg
 35 40 45
 5 Tyr Glu Pro Gly Val Ser Val Gly Gly Ala Gly Gln Arg Ala Gly Ile
 50 55 60
 10 Thr Gly Tyr Asn Ile Arg Gly Ile Asp Gly Asn Arg Ile Leu Thr Gln
 65 70 75 80
 15 Ile Asp Gly Val Glu Leu Pro Asn Asp Phe Phe Ser Gly Pro Tyr Ala
 85 90 95
 20 Gln Thr His Arg Asn Tyr Val Asp Pro Asp Ile Val Lys Arg Val Glu
 100 105 110
 25 Ile Leu Arg Gly Pro Ala Ser Ala Leu Tyr Gly Ser Asn Ala Ile Gly
 115 120 125
 30 Gly Ala Val Ser Tyr Phe Thr Leu Asp Pro Ser Asp Ile Ile Lys Asp
 130 135 140
 35 Gly Lys Asp Val Gly Ala Arg Leu Lys Ala Gly Tyr Glu Ser Ala Ser
 145 150 155 160
 40 His Ser Trp Leu Thr Ser Ala Thr Val Ala Gly Arg Ala Asp Asp Phe
 165 170 175
 45 Asp Gly Leu Leu His Tyr Gly Tyr Arg Gln Gly His Glu Thr Glu Ser
 180 185 190
 50 Asn Gly Gly His Gly Gly Thr Gly Leu Ser Arg Ser Glu Ala Asn Pro
 195 200 205
 55 Glu Asp Ala Asp Ser Tyr Ser Leu Leu Gly Lys Leu Gly Trp Asn Tyr
 210 215 220
 60 Ala Glu Gly Ser Arg Phe Gly Leu Val Phe Glu Lys Tyr Lys Ser Asp
 225 230 235 240
 65 Val Asp Thr Asp Gln Lys Ser Ala Tyr Gly Gly Pro Tyr Asp Lys Gly
 245 250 255
 70 Lys Pro Ala Ile Pro Pro Ser Met Leu Pro Gly Gly Met Tyr Gln Trp
 260 265 270
 75 Arg Lys Gly Asn Asp Thr Leu Thr Arg Glu Arg Tyr Gly Leu Glu His

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	275					280					285					
5	His	Phe	Leu	Leu	Asp	Ser	Gln	Val	Ala	Asp	Arg	Ile	Gln	Trp	Ser	Leu
		290					295					300				
10	Asn	Tyr	Gln	Leu	Ala	Lys	Thr	Asp	Gln	Ala	Thr	Arg	Glu	Phe	Tyr	Tyr
	305					310					315					320
15	Pro	Ile	Thr	Arg	Lys	Val	Leu	Arg	Thr	Arg	Asp	Thr	Thr	Tyr	Lys	Glu
					325					330					335	
20	Arg	Leu	Trp	Val	Phe	Asp	Ser	Gln	Leu	Asp	Lys	Ser	Phe	Ala	Ile	Gly
				340					345					350		
25	Glu	Thr	Glu	His	Leu	Leu	Ser	Tyr	Gly	Ile	Asn	Leu	Lys	His	Gln	Lys
			355					360					365			
30	Val	Thr	Gly	Met	Arg	Ser	Gly	Thr	Gly	Thr	Asn	Leu	Asp	Thr	Gly	Ala
		370					375					380				
35	Asp	Ser	Pro	Arg	Asp	Ala	Leu	Glu	Arg	Ser	Ser	Asp	Phe	Pro	Asp	Pro
	385					390					395					400
40	Thr	Val	Lys	Thr	Tyr	Ala	Leu	Phe	Ala	Gln	Asp	Ser	Ile	Ser	Trp	Asn
					405					410					415	
45	Asp	Trp	Thr	Phe	Thr	Pro	Gly	Leu	Arg	Tyr	Asp	Tyr	Thr	Arg	Met	Glu
				420					425					430		
50	Pro	His	Ile	Thr	Asp	Glu	Phe	Leu	Arg	Thr	Met	Lys	Gln	Ser	Gln	Asn
			435					440					445			
55	Thr	Ala	Val	Asp	Glu	Ser	Asp	Lys	Lys	Trp	His	Arg	Val	Ser	Pro	Lys
		450					455					460				
60	Phe	Gly	Val	Thr	Tyr	Asp	Phe	Ala	Gln	His	Tyr	Thr	Trp	Tyr	Gly	Gln
	465					470					475					480
65	Tyr	Ala	Gln	Gly	Phe	Arg	Thr	Pro	Thr	Ala	Lys	Ala	Leu	Tyr	Gly	Arg
					485					490					495	
70	Phe	Glu	Asn	Leu	Gln	Ala	Gly	Tyr	His	Ile	Glu	Pro	Asn	Pro	Asn	Leu
				500					505					510		
75	Lys	Pro	Glu	Lys	Ser	Gln	Ser	Phe	Glu	Thr	Gly	Leu	Arg	Gly	Lys	Phe
			515					520					525			

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Asp Glu Gly Ser Phe Gly Val Ala Val Phe Tyr Asn Lys Tyr Arg Asp
 530 535 540

5
 Phe Ile Asp Glu Asp Ala Leu Asn Thr Asp Ser Thr Gly Gly Asn Gly
 545 550 555 560

10
 Gln Thr Phe Gln Ser Asn Asn Ile Glu Arg Ala Val Ile Lys Gly Val
 565 570 575

15
 Glu Leu Lys Gly Arg Leu Glu Leu Gly Ala Phe Gly Ala Pro Gln Gly
 580 585 590

20
 Leu Tyr Thr Gln Gly Ser Val Ala Tyr Ala Tyr Gly Arg Asn Lys Asp
 595 600 605

25
 Asn Gly Glu Pro Ile Asn Ser Val Asn Pro Leu Thr Gly Val Phe Gly
 610 615 620

30
 Leu Gly Tyr Asp Glu Ala Asp Gly Asn Tyr Gly Gly Leu Leu Ser Trp
 625 630 635 640

35
 Thr Leu Val Lys Arg Lys Asp Arg Val Asp Asp Ser Thr Phe His Thr
 645 650 655

40
 Pro Asp Gly Thr Ala Ser Gln Phe Lys Thr Pro Gly Phe Gly Val Leu
 660 665 670

45
 Asp Leu Ser Ala Tyr Tyr Arg Leu Ser Lys Asp Leu Thr Leu Asn Ala
 675 680 685

50
 Gly Leu Tyr Asn Leu Thr Asp Lys Lys Tyr Trp Leu Trp Asp Asp Val
 690 695 700

55
 Arg Gly Tyr Asp Ser Val Gly Glu Ala Ser Ala Leu Ala Pro Ala Asn
 705 710 715 720

Ile Asp Arg Leu Ser Gln Pro Gly Arg Asn Phe Ala Val Asn Leu Val
 725 730 735

Trp Asp Ile

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 <211> 1069
 <212> PRT
 <213> Pseudomonas aeruginosa

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				20					25					30		
	Ile	Glu	Phe	Asn	Pro	Phe	Ser	Leu	Glu	Leu	Thr	Leu	Trp	Gly	Leu	Arg
10			35					40					45			
	Leu	Gly	Glu	Glu	Lys	Asn	Pro	Gln	Leu	Ala	Phe	Arg	Arg	Leu	Tyr	Ala
		50					55					60				
15	Asn	Leu	Gln	Leu	Asp	Ser	Leu	Trp	Lys	Arg	Gln	Leu	His	Leu	Ala	Asp
	65					70					75					80
	Val	Glu	Leu	Glu	Gly	Pro	His	Thr	Glu	Leu	Leu	Phe	Gly	Glu	Lys	Gly
20					85					90					95	
	Gln	Leu	Asn	Leu	Ala	Ser	Leu	Phe	Arg	Ile	Pro	Pro	Ser	Glu	Ser	Pro
25				100					105					110		
	Glu	Pro	Glu	Gln	Pro	Ser	Asp	Pro	Phe	Pro	Leu	Arg	Ile	Asp	Arg	Ile
			115					120					125			
30	Gln	Leu	Ala	Glu	Gly	Ser	Leu	His	Phe	Gln	Asp	Leu	Arg	Pro	Ser	Glu
		130					135					140				
	Pro	Val	Asp	Phe	Ser	Phe	Asp	Pro	Leu	Gly	Phe	Glu	Leu	His	Asn	Leu
35	145					150					155					160
	Ser	Thr	Leu	Pro	Asp	Asp	Gly	Ala	Lys	Met	Thr	Leu	Val	Ala	Thr	Gly
					165					170					175	
40	Pro	Asn	Gly	Gly	Arg	Leu	Asp	Trp	Glu	Gly	Asp	Leu	Thr	Leu	Val	Pro
			180						185					190		
45	Ile	Thr	Ser	Arg	Gly	His	Leu	Ser	Val	Lys	Asp	Ile	Gln	Leu	Lys	Ala
			195					200					205			
	Trp	Trp	Pro	Tyr	Val	Arg	Asp	Asn	Ala	Pro	Leu	Val	Leu	Glu	Asn	Gly
50		210					215					220				
	Val	Val	Ser	Leu	Ser	Ser	Asp	Tyr	Arg	Leu	Asp	Leu	Ser	Lys	Asp	Thr
	225					230					235					240
55	Gln	Leu	Leu	Leu	Asp	Lys	Ala	Ala	Leu	Lys	Leu	Ala	Asp	Phe	Ser	Ile
				245						250					255	

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Asn Ser Pro Gln Gly Lys Pro Leu Ala Lys Leu Ala Ser Leu Asp Val
260 265 270

5 Ala Ala Thr Thr Leu Asp Leu Ala Lys Gln Glu Val Val Leu Gly Glu
275 280 285

10 Val Arg Ser Gln Gly Leu Glu Ala Trp Ala Ala Arg Glu Lys Asp Gly
290 295 300

15 Gln Leu Asp Trp Gln Lys Leu Phe Ala Asp Phe Thr Pro Pro Pro Arg
305 310 315 320

Lys Ala Pro Ala Pro Lys Pro Ala Glu Asn Thr Asp Pro Ala Ala Ala
325 330 335

20 Pro Thr Asp Ala Ala Lys Thr Thr Ser Glu Pro Ala Thr Asp Gly Ala
340 345 350

25 Ala Lys Ala Ala Ala Ile Ala Ser Gly Glu Ala Ser Lys Asp Arg Pro
355 360 365

30 Ala Glu Lys Asp Ala Ser Val Ala Glu Thr Glu Arg Ala Thr Asp Asp
370 375 380

Lys Glu Ser Ala Lys Ala Ala Glu Gly Ala Ala Asp Lys Val Ala Lys
385 390 395 400

35 Gln Glu Thr Ser Lys Ala Pro Lys Thr Gly Lys Ala Thr Gly Gln Glu
405 410 415

40 Thr Ala Lys Thr Ala Glu Ile Asp Lys Ala Ala Ser Asp Ser Pro Gln
420 425 430

Gln Leu Ala Asp Thr Ala Lys Thr Pro Pro Pro Glu Ser Thr Lys Ala
435 440 445

45 Ser Ala Glu Thr Pro Ala Lys Pro Trp Asn Ile Val Leu Arg Asp Ala
450 455 460

50 Gln Leu Arg Gly Tyr Lys Ala His Leu Val Asp Arg Gln Pro Ala Thr
465 470 475 480

Glu Val Pro Leu Glu Val Gly Pro Leu Asp Leu Asp Leu Gln Asn Val
485 490 495

55 Asp Ser Leu Gly Lys Thr Pro Phe Asp Leu Lys Leu Lys Thr Gly Leu
500 505 510

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Gly Asn Arg Gly Gln Val Gln Ala Ser Gly Gln Val Val Leu Asp Pro
 515 520 525
 5 Val Ser Ala Arg Leu Lys Val Ser Thr Arg Asp Ile Asp Leu Arg Val
 530 535 540
 10 Ala Gln Ala Tyr Ile Ser Pro Phe Ile Arg Leu Glu Leu Arg Ser Gly
 545 550 555 560
 Phe Leu Gly Ser Glu Leu Ala Val Asp Leu Lys Ser Val Glu Pro Leu
 565 570 575
 15 Ala Phe Ser Val Asp Gly Ser Ala Glu Val Ser Gln Leu His Thr Leu
 580 585 590
 20 Asp Thr Ile Lys Asp Arg Asp Phe Val Lys Trp Thr Lys Leu Thr Leu
 595 600 605
 Asn Gly Leu Ala Tyr Arg His Glu Asp Ser Leu Ser Ile Gln Ser Val
 610 615 620
 25 Ser Phe Glu Glu Pro Tyr Ala Arg Phe Ile Ile Asn Glu Asp Arg Ser
 625 630 635 640
 30 Thr Asn Val Ser Glu Leu Ile Ile Pro Gln Pro Ala Ser Ser Ser Gly
 645 650 655
 35 Lys Thr Ala Ala Glu Ser Lys Asn Ala Pro Ala Ser Lys Pro Leu Gly
 660 665 670
 40 Ile His Ile Gly Gly Val Arg Ile Asn Asn Gly Ser Ala Asn Phe Ala
 675 680 685
 Asp Leu Thr Leu Met Pro Pro Phe Gly Thr Ala Ile Gln Gln Leu Ser
 690 695 700
 45 Gly Glu Val Gly Thr Leu Asp Thr Arg Asn Ser Gln Pro Ala Lys Val
 705 710 715 720
 50 Asp Ile Lys Gly Lys Val Asp Lys Tyr Ala Pro Val Thr Ile Ala Gly
 725 730 735
 Glu Leu Asp Pro Phe Asp Pro Leu Lys Lys Leu Asp Ile Thr Thr Ser
 740 745 750
 55 Phe Lys Arg Val Glu Leu Thr Thr Leu Thr Pro Tyr Ser Gly Lys Phe
 755 760 765

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Ala Gly Tyr Arg Ile Arg Lys Gly Arg Leu Asn Leu Asp Leu His Tyr
770 775 780

5 Gln Ile Glu Arg Ser Gln Leu Lys Ala Glu Asn Lys Val Leu Leu Glu
785 790 795 800

10 Gly Leu Gln Leu Gly Glu Lys Val Asp Ser Pro Asp Ala Val Asp Leu
805 810 815

15 Pro Val Lys Leu Ala Val Ala Leu Leu Lys Asp Thr Lys Gly Asn Ile
820 825 830

20 Asp Ile Gln Leu Pro Val Ala Gly Asp Leu Asn Asn Pro Glu Phe Ser
835 840 845

25 Val Met Pro Ile Val Trp Gln Thr Leu Arg Asn Leu Val Leu Arg Ala
850 855 860

30 Val Gln Ala Pro Phe Lys Phe Ile Ala Gly Leu Ala Ala Gly Gly Asn
865 870 875 880

35 Glu Asp Leu Gly Thr Val Pro Phe Ala Ala Gly Ser Asp Glu Leu Thr
885 890 895

40 Pro Glu Ala Gln Ala Asn Leu Asp Lys Leu Ala Asp Ala Leu Lys Glu
900 905 910

45 Arg Pro Ala Leu Arg Leu Glu Val Glu Gly Val Ala Ser Ala Ala Ala
915 920 925

50 Asp Gly Pro Ser Ile Gly Ala Lys Arg Leu Glu Leu Glu Tyr Gln Asn
930 935 940

55 Thr Tyr Tyr Arg Met Leu Gln Arg Arg Gly Asp Lys Val Pro Ser Asp
945 950 955 960

60 Ala Lys Gln Leu Glu Val Pro Glu Asn Met Gln Ala Pro Leu Leu Glu
965 970 975

65 Gly Ile Tyr Arg Thr Arg Leu Lys Gln Gln Pro Pro Ala Glu Trp Lys
980 985 990

70 Glu Leu Asp Ser Asp Glu Arg Thr Ala Lys Met Arg Glu Ala Val Ile
995 1000 1005

75 Ala Ser Trp Ala Lys Ser Gln Val Leu Leu Arg Gln Ile Gly Gln

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1010 1015 1020

5 Ala Arg Ala Thr Arg Ile Lys Asp Tyr Leu Val Glu Lys Gly Gln
1025 1030 1035

10 Leu Pro Asp Asp Arg Ile Tyr Leu Ile Asp Val Ser Phe Ala Glu
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20 Glu

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25 <400> 52
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30 Asp Ala Ala Lys Gln Tyr Ala Val Asp Ala Glu Lys Lys Phe Gly Pro
20 25 30

35 Gln Leu Asn Lys Leu Lys Asn Leu Glu Arg Asp Ala Lys Ala Leu Gln
35 40 45

40 Asp Lys Leu Val Ser Asn Gly Ser Lys Met Ser Gln Gly Asp Arg Glu
50 55 60

45 Lys Ala Glu Leu Asp Phe Lys Gln Lys Ala Arg Asp Phe Gln Phe Gln
65 70 75 80

50 Ser Lys Glu Leu Asn Glu Ser Lys Ala Ala Ala Asp Arg Asp Met Leu
85 90 95

55 Lys Lys Leu Lys Pro Lys Leu Asp Gln Ala Val Glu Glu Thr Ile Lys
100 105 110

60 Lys Gly Gly Tyr Asp Met Val Ile Glu Arg Gly Ala Val Val Asp Val
115 120 125

65 Lys Pro Gln Tyr Asp Ile Thr Arg Gln Val Ile Glu Arg Met Asn Gln
130 135 140

70 Leu Arg
145

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<210> 53
 <211> 187
 <212> PRT
 <213> Pseudomonas aeruginosa

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Glu Arg Gly Phe Asp Lys Pro Ala Cys Ala Ser Ser Thr Leu Phe Lys
 20 25 30

15

Thr Phe Pro Val Thr Leu Ser Asp Ser Phe Ser Gly Pro Gly Pro Ala
 35 40 45

20

Lys Gly Asn Ala Ala Val Tyr Asp Ala Leu Val Gly Val Gly Leu Leu
 50 55 60

25

Arg Arg Asp Gly Asp Ser Tyr Asp Leu Thr Pro Ala Gly Arg Glu Asp
 65 70 75 80

30

Tyr Lys Pro Glu Ser Lys Ala Phe Cys Tyr Ser Ser Gly Phe Asp Val
 85 90 95

Ser Val Arg Ser Val Asp Pro Ala Lys Pro Asp Asp Tyr Gly Pro Ala
 100 105 110

35

Val Glu Lys Gly Trp Leu Val Thr Val Glu Val Lys Pro Arg Glu Val
 115 120 125

Lys Asp Trp Ala Lys Asn Pro Glu Val Leu Lys Gln Ala Ser Leu Thr
 130 135 140

40

Thr Leu Gln Gln Ile Thr Gln Pro Gln Val Gly Gln Val Ser Leu Val
 145 150 155 160

45

Lys Pro Arg Gly Glu Glu Gly Tyr Lys Leu Val Asn Thr Arg Phe Ser
 165 170 175

Pro Arg Gln Gly Phe His Phe Asn Gln Ala Trp
 180 185

50

<210> 54
 <211> 427
 <212> PRT
 <213> Pseudomonas aeruginosa

55

<400> 54
 Gly Asp Gly Gly Phe Val Glu Asp Ser Glu Leu Gln Phe Leu Ala Arg

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				20				25					30			
10	Arg	Asn	Arg	Phe	Lys	Pro	Arg	Ser	Glu	Arg	Asn	Gly	Tyr	Arg	Glu	Glu
			35					40					45			
15	Ala	Thr	Gln	Gly	Leu	Arg	Leu	Gln	Phe	Ala	Ser	Gly	Tyr	Thr	Pro	Gly
		50					55					60				
20	Ser	Leu	Gly	Phe	Gly	Leu	Asp	Ala	His	Ala	Met	Leu	Gly	Leu	Gln	Leu
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25	Asp	Ser	Gly	Gly	Gly	Arg	Thr	Gly	Thr	Gly	Asn	Leu	Pro	Val	Gly	Ala
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30	Asp	Gly	His	Pro	Asp	His	Arg	Tyr	Gly	Lys	Val	Gly	Gly	Ala	Leu	Arg
			100						105					110		
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45	Tyr	Gly	Leu	Leu	Leu	Glu	Asp	Arg	Ser	Phe	Asp	Gly	Leu	Leu	Leu	Glu
	145					150					155					160
50	Gly	Gly	Arg	Phe	Thr	Ala	Ala	Ser	Gly	Pro	Gly	Glu	Ser	Lys	Val	Arg
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55	Gly	Asp	Ile	Ser	Thr	Val	Tyr	Gly	Arg	Leu	Gly	Ala	Tyr	Pro	Val	Arg
				180					185					190		
60	Leu	Asp	Ala	Val	Gly	Phe	Leu	Gly	Gly	Gln	Trp	Gln	Ala	Thr	Glu	Arg
			195					200					205			
65	Leu	Gln	Leu	Ser	Leu	Tyr	Ala	Ser	Arg	Phe	Asp	Asp	Ile	Trp	Gln	Gln
		210					215					220				
70	Ala	Tyr	Phe	Gly	Ala	Ser	His	Arg	Gln	Pro	Leu	Gly	Gly	Glu	Arg	Ala
	225					230					235					240
75	Leu	Arg	Val	Asp	Leu	Asp	Ala	Tyr	Arg	Thr	Arg	Asp	Ser	Gly	Gln	Ser
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Arg Phe Gly Arg Ile Asp Thr Leu Thr Ser Ser Leu Ala Leu Gly Tyr
 260 265 270
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 Glu His Gly Pro Gln Arg Ile Thr Leu Ala Tyr Gln Arg Val His Gly
 275 280 285
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 Glu Gln Pro Phe Asp Tyr Met Ala Phe Gly Asp Gly Arg Ser Ser Ala
 290 295 300
 Ser Met Val Leu Ala Asn Ser Val Gly Tyr Ser Asp Phe Asn Gly Pro
 305 310 315 320
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 Gly Glu Arg Ser Trp Gln Leu Arg Tyr Asp Leu Asp Leu Gly Ala Leu
 325 330 335
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 Gly Leu Pro Gly Leu Ser Leu His Ala Leu His Ala Arg Gly Arg Ala
 340 345 350
 Gly Ala Ser Ala Ser Ser Ala Ala Glu Ser Ile Tyr Ala Gly Leu Tyr
 355 360 365
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 Gly Arg Asp Gly Arg His Arg Glu Asn Asp Leu Gly Phe Ala Tyr Arg
 370 375 380
 30
 Val Lys Ala Gly Pro Leu Ala Gly Leu Ala Leu Arg Ala Ser Gln Ala
 385 390 395 400
 Trp His Arg Gly Asn Ala Ser Tyr Leu Asp Gly Asp Ile Asp Glu Thr
 405 410 415
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 420 425
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 20 25 30
 Glu Gln His Ala Ala Gln Leu Glu Lys Asp Leu Ala Ser Leu Asp Arg
 35 40 45
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 Ala Leu Ala Ala Ala Pro Glu Gly Val Leu Leu Arg Gln Gly Glu Lys

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5	Thr 65	Leu	Val	Ala	Arg	Ile 70	Arg	Glu	Gly	Ala	Ala 75	Tyr	Gly	Pro	Arg	Glu 80			
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	Asp	Phe	Leu	Asn 100	Leu	Val	Glu	Arg	Gln 105	Val	Pro	Pro	Pro	Pro	Pro	Gly 110			
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	Leu	Gln	Tyr	Leu	Ala	Arg	Ala 135	Tyr	Leu	Gly	Gly	Leu	Glu	Thr	Ala	Arg 140			
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Leu Thr Gln Val Thr Glu Ala Arg Ala Lys Val Gly Ser Val Gln Leu
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5 Asn Ala Asp Gln Leu Asp Asp Glu Gln Ala Val Gln Arg Phe Gln Lys
 65 70 75 80

10 Ala Gln Gly Glu Leu Ser Ser Ala Leu Ser Arg Leu Leu Val Val Thr
 85 90 95

15 Glu Asn Tyr Pro Gln Leu Lys Ala Asp Gly Leu Phe Lys Asp Leu Leu
 100 105 110

Thr Gln Leu Glu Gly Thr Glu Asn Arg Ile Ala Val Ala Arg Gly Arg
 115 120 125

20 Tyr Val Lys Ser Val Gln Glu Tyr Asn Val Leu Leu Arg Gln Phe Pro
 130 135 140

25 Gly Val Ile Thr Ala Lys Leu Phe Gly Tyr Lys Pro Lys Ala Asn Phe
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Ser Val Glu Asn Glu Ala Ala Ile Ser Thr Ala Pro Lys Val Asp Phe
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30 Gly Asn Pro Gln Pro Ala Gln
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 <213> Pseudomonas aeruginosa

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Tyr Asp Asp Gly Trp Arg Ser Glu Arg Arg Tyr Tyr Ser Thr Arg Tyr
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50 Tyr Asp Gln Arg Tyr Tyr Pro Ala Pro Arg Arg Tyr Asp Gly His Arg
 50 55 60

55 Asp Tyr Arg Arg Glu Gln Tyr Arg Tyr Gln Gln Arg Tyr His Glu Ser
 65 70 75 80

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Arg Pro Ala His Arg Gly Glu Arg His Pro Gly Asn Trp Gln Arg Gly
 85 90 95
 5 Gly Gln Pro Gln Trp Arg Gly His Ser Pro Gln Arg Trp Gln Gln His
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 35 40 45
 Gly Ala Gly Tyr Met Gly Ser Gly Ser Gln Ile Val Asp Val Arg Arg
 50 55 60
 35 Leu Ala Ser Asp Phe Leu Thr Gly Gln Leu Arg Asn Ala Thr Ser Gln
 65 70 75 80
 40 Asn Ser Glu Leu Asn Ala Phe Leu Gly Gln Ile Asp Gln Leu Asn Ser
 85 90 95
 45 Leu Leu Ala Asp Asn Thr Thr Gly Val Ser Pro Ala Met Gln Arg Phe
 100 105 110
 Phe Ser Ala Leu Gln Thr Ala Ala Gln Asn Pro Ser Ser Thr Glu Ala
 115 120 125
 50 Arg Glu Ala Val Leu Ala Gln Ala Gln Gly Leu Ser Lys Thr Phe Asn
 130 135 140
 55 Thr Leu Tyr Asp Gln Leu Asp Lys Gln Asn Ser Leu Ile Asn Gln Gln
 145 150 155 160

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Leu Gly Ala Leu Thr Ser Gln Val Asn Asn Leu Ser Gln Ser Val Ala
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 Glu Tyr Asn Asp Ala Ile Ala Lys Ala Lys Ser Ala Gly Ala Val Pro
 180 185 190
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 Asn Asp Leu Leu Asp Ala Arg Asp Glu Ala Val Arg Lys Leu Ser Glu
 195 200 205
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 Met Val Gly Val Thr Ala Val Thr Gln Asp Asp Asn Ser Val Ser Leu
 210 215 220
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 Phe Ile Gly Ser Gly Gln Pro Leu Val Val Gly Asn Thr Val Ser Thr
 225 230 235 240
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 Leu Ser Val Val Pro Gly Leu Asp Asp Pro Thr Arg Tyr Gln Val Gln
 245 250 255
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 Leu Thr Leu Gly Asp Ser Thr Gln Asn Val Thr Arg Leu Val Ser Gly
 260 265 270
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 Gly Gln Met Gly Gly Leu Leu Ala Tyr Arg Asp Thr Val Leu Asp Ser
 275 280 285
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 Ser Tyr Asn Lys Leu Gly Gln Leu Ala Leu Thr Phe Ala Asp Thr Val
 290 295 300
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 Asn Leu Phe Gly Asp Ile Asn Asp Pro Asp Ile Thr Ala Leu Arg Val
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 Thr Asp Thr Ser Lys Leu Asn Ser Ser Asp Phe Arg Leu Asp Phe Asp
 355 360 365
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 Gly Thr Asn Phe Thr Ala Arg Arg Leu Gly Asp Asp Ala Ser Met Gln
 370 375 380
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 Val Thr Val Ser Gly Thr Gly Pro Tyr Thr Leu Ser Phe Lys Asp Ala
 385 390 395 400
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 Asn Gly Val Asp Gln Gly Phe Ser Val Thr Leu Asp Gln Leu Pro Ala
 405 410 415

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Ala Gly Asp Arg Phe Thr Leu Gln Pro Thr Arg Arg Gly Ala Ser Asp
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5 Ile Glu Thr Thr Leu Lys Asn Ala Ser Gln Leu Ala Phe Ala Gly Ser
435 440 445

Ala Arg Ala Glu Ala Thr Thr Asn Asn Arg Gly Ser Gly Ala Ile Gly
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Gln Pro Asn Leu Val Asp Gly Pro Ser Pro Ile Asp Pro Ala Val Leu
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Gln Asn Ala Phe Gly Ala Asn Gly Leu Pro Leu Ser Ala Thr Val Ser
485 490 495

Ala Asp Gly Lys Thr Tyr Thr Met Thr Ser Pro Leu Pro Ala Gly Trp
20 500 505 510

Ser Tyr Val Asp Lys Asp Gly Asn Ala Leu Pro Gly Ser Pro Thr Leu
25 515 520 525

Asn Ser Gly Thr Ser Asn Ser Val Arg Met Ala Tyr Thr Asp Pro Gly
30 530 535 540 560

Ser Gly Gln Thr Tyr Thr Tyr Glu Phe Asn Leu Ser Asn Val Pro Gln
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Thr Gly Asp Ser Phe Thr Leu Ser Phe Asn Lys Asp Gly Ile Ala Asp
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Asn Arg Asn Ala Leu Asn Leu Asn Ala Leu Gln Thr Lys Pro Thr Val
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Gly Gly Thr Asp Ser Thr Gly Ser Thr Tyr Asn Asp Ala Tyr Gly Gly
595 600 605

Leu Val Glu Arg Val Gly Thr Leu Thr Ala Gln Ala Arg Ala Ser Ala
45 610 615 620

Asp Ala Ser Gln Thr Val Leu Lys Gln Ala Gln Asp Ser Arg Asp Ser
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Leu Ser Gly Val Ser Leu Asp Glu Glu Ala Ala Asn Leu Ile Gln Phe
645 650 655

55 Gln Gln Tyr Tyr Ser Ala Ser Ala Gln Val Ile Gln Val Ala Arg Ser
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25 Ile Gly Asn Trp Thr Ser Asn Leu Asp Pro Gly Lys Pro Thr Glu Ile
 50 55 60

30 Asp Ser Tyr Ala Gly Phe Lys Arg Pro Leu Asn Asn Arg Leu Gly Tyr
 65 70 75 80

35 Glu Met Gly Leu Ile Arg Tyr Ser Arg Pro Glu Gln Pro Ala Asn Asp
 85 90 95

40 Ala Ala Glu Leu Tyr Gly Gly Leu Ser Ile Phe Gly Ser Arg Leu Gly
 100 105 110

45 Ala Ala Leu Ser Ser Asp Pro Gly Arg Asn Asp Thr Thr Leu Phe Ala
 115 120 125

50 Asp Leu Gly Val Asn Pro Pro Phe Gly Phe Asp Val Thr Leu Lys Tyr
 130 135 140

55 Gly Asn His Arg Leu Asp Asn Pro Ala Ser Leu Ser Gly Gly Gly Tyr
 145 150 155 160

60 Val Ser Val Phe Asn Asp Trp Ser Val Asn Leu Ser Arg Pro Trp Leu
 165 170 175

65 Gly Ile Asp Leu Asn Leu Ser Tyr Ser Gly Thr Ser Leu Thr Gly Ser
 180 185 190

70 Asp Cys Ser Ala Tyr Ser Gly His Asn Ser Tyr Cys Asp Thr Thr Phe
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20 Leu Thr Ser Ala Ser Gly Ala Ile Gln Lys Gly Thr Asn Thr Lys Val
 35 40 45

25 Ala Leu Glu Pro Ala Thr Ser Tyr Met Lys Ala Tyr Tyr Ala Lys Phe
 50 55 60

30 Gly Asn Leu Asp Ala Ala Lys Arg Asp Pro Asp Val Gln Pro Pro Val
 65 70 75 80

35 Leu Asp Pro Arg Arg Ala Thr Tyr Val Arg Glu Ala Thr Thr Asp Gln
 85 90 95

40 Asn Gly Arg Phe Asp Phe Asp His Ile Pro Asn Gly Thr Tyr Tyr Ile
 100 105 110

45 Ser Ser Glu Leu Thr Trp Ser Ala Gln Ser Asp Gly Lys Thr Ile Thr
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50 Glu Gly Gly Thr Val Thr Lys Leu Val Thr Val Ser Gly Ser Gln Pro
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55 Gln Lys Val Leu Leu Thr Arg
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 <211> 326
 <212> PRT
 <213> Pseudomonas aeruginosa

65 <400> 61
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70 Thr Asp Ser Val Arg Asn Met Lys Asn Ala Asp Leu Tyr Gly Gly Ser
 20 25 30

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Ile Gly Tyr Phe Leu Thr Asp Asp Val Glu Leu Ala Leu Ser Tyr Gly
 35 40 45

5 Glu Tyr His Asp Val Arg Gly Thr Tyr Glu Thr Gly Asn Lys Lys Val
 50 55 60

10 His Gly Asn Leu Thr Ser Leu Asp Ala Ile Tyr His Phe Gly Thr Pro
 65 70 75 80

15 Gly Val Gly Leu Arg Pro Tyr Val Ser Ala Gly Leu Ala His Gln Asn
 85 90 95

Ile Thr Asn Ile Asn Ser Asp Ser Gln Gly Arg Gln Gln Met Thr Met
 100 105 110

20 Ala Asn Ile Gly Ala Gly Leu Lys Tyr Tyr Phe Thr Glu Asn Phe Phe
 115 120 125

25 Ala Lys Ala Ser Leu Asp Gly Gln Tyr Gly Leu Glu Lys Arg Asp Asn
 130 135 140

Gly His Gln Gly Glu Trp Met Ala Gly Leu Gly Val Gly Phe Asn Phe
 145 150 155 160

30 Gly Gly Ser Lys Ala Ala Pro Ala Pro Glu Pro Val Ala Asp Val Cys
 165 170 175

35 Ser Asp Ser Asp Asn Asp Gly Val Cys Asp Asn Val Asp Lys Cys Pro
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40 Asp Thr Pro Ala Asn Val Thr Val Asp Ala Asn Gly Cys Pro Ala Val
 195 200 205

45 Ala Glu Val Val Arg Val Gln Leu Asp Val Lys Phe Asp Phe Asp Lys
 210 215 220

Ser Lys Val Lys Glu Asn Ser Tyr Ala Asp Ile Lys Asn Leu Ala Asp
 225 230 235 240

50 Phe Met Lys Gln Tyr Pro Ser Thr Ser Thr Thr Val Glu Gly His Thr
 245 250 255

55 Asp Ser Val Gly Thr Asp Ala Tyr Asn Gln Lys Leu Ser Glu Arg Arg
 260 265 270

Ala Asn Ala Val Arg Asp Val Leu Val Asn Glu Tyr Gly Val Glu Gly

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	Asn	Ala	Thr	Ala	Glu	Gly	Arg	Ala	Ile	Asn	Arg	Arg	Val	Glu	Ala	Glu	
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	<211>	324															
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30	Met	Ala	Val	Val	Leu	Val	Ala	Asp	Val	Met	Pro	His	Lys	Ser	Leu	Ser	
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70	Ser	Glu	Ile	Lys	Thr	Glu	Lys	Val	Cys	Thr	Ala	Val	His	Val	Ala	Ser	
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Gly Ala Cys Val Ser Trp Gly Glu Gln Gln Tyr Thr Gln Thr Thr Gln
 180 185 190
 5 Gly Ser Gln Ala Gly Tyr Tyr Gln Gln Thr Asp Ser Arg Asp Val Pro
 195 200 205
 10 Ser Ile Lys Val Gln Ala Arg Leu Pro Val Asp Lys Ala Leu Ala Ser
 210 215 220
 Phe Thr Val Gln Gly Gly Gln Leu Leu Leu Ala Pro Arg Met His Leu
 225 230 235 240
 15 Lys Thr Pro Gly Tyr Lys Tyr Gln Gln Ser Lys Cys Arg Ala Ile Asp
 245 250 255
 20 Pro Lys Lys Ile Glu Cys Pro Leu Glu Asn Leu Thr Val Tyr Thr Trp
 260 265 270
 25 Pro Ala Pro Met Asp Phe Ser Gln Ser Leu Ile Ala Gln Arg Ala Leu
 275 280 285
 30 Ser Asp Lys His Arg Gln Leu Leu Ser Arg Leu Gln Pro Leu Gln Ile
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 55 Asp Ser Gly Phe Asp Pro Ser His Pro Asp Thr Pro Ala Ser Arg Tyr
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5 Gln Pro Val Thr Ala Ser Gly Thr Tyr Val Asp Gly Thr Pro Phe Ser
 65 70 75 80
 Val Ser Gly Ala Met Asn Gly Asn Asn Asp Ser His Gly Thr His Val
 85 90 95
 10 Gly Gly Thr Leu Gly Ala Ser Arg Asp Gly Val Gly Met His Gly Val
 100 105 110
 Ala Tyr Ala Ala Gln Val Tyr Val Ala Asn Thr Asn Gln Asn Asp Ser
 115 120 125
 15 Phe Leu Phe Gly Pro Thr Pro Asp Pro Asn Tyr Phe Lys Ala Ala Tyr
 130 135 140
 20 Gln Ala Leu Ala Asp Ala Gly Val Arg Ala Ile Asn Asn Ser Trp Gly
 145 150 155 160
 Ser Gln Pro Lys Asp Val Ser Tyr Glu Thr Leu Asp Gly Leu His Ala
 165 170 175
 25 Ala Tyr Ala Gln His Tyr Gly Arg Ser Thr Trp Leu Asp Ala Ala Ala
 180 185 190
 30 Gly Val Ser Arg Gln Gly Val Ile Asn Val Phe Ser Ala Gly Asn Ser
 195 200 205
 35 Gly Tyr Ala Asn Ala Ser Val Arg Ser Ala Leu Pro Tyr Phe Gln Pro
 210 215 220
 Asp Leu Glu Gly His Trp Leu Ala Val Ser Gly Leu Asp Gln Gln Asn
 225 230 235 240
 40 Gly Gln Arg Tyr Asn Arg Cys Gly Ile Ala Lys Tyr Trp Cys Ile Thr
 245 250 255
 45 Thr Pro Gly Arg Leu Ile Asn Ser Thr Met Pro Gly Gly Gly Tyr Ala
 260 265 270
 50 Asn Lys Ser Gly Thr Ser Met Ala Ala Pro His Ala Thr Gly Ala Leu
 275 280 285
 Ala Leu Val Met Gln Arg Tyr Pro Tyr Leu Asn Asn Glu Gln Ala Leu
 290 295 300
 55 Gln Val Leu Leu Thr Thr Ala Thr Gln Leu Asp Gly Thr Pro Thr Gly
 305 310 315 320

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Ala Pro Thr Asp Thr Val Gly Trp Gly Val Pro Asp Leu Gly Arg Ala
 325 330 335

5 Met His Gly Pro Gly Gln Leu Leu Gly Arg Phe Glu Ala Asn Leu Pro
 340 345 350

10 Ala Gly Leu Arg Asp Glu Trp Ser Asn Pro Ile Ser Asp Ser Ala Leu
 355 360 365

15 Leu Gln Arg Gln Ala Glu Asp Ala Ala Glu His Ala Ala Trp Gln Arg
 370 375 380

Thr Leu Lys Asp Lys Gly Trp Glu Asn Gly Leu Pro Ala Gly Ala Ser
 385 390 395 400

20 Gln Gln Glu Arg Thr Asp Tyr Ala Ile Gly Met Ala Arg Asp Gln Ala
 405 410 415

25 Ala Ala Gln Arg Gln Tyr Gln Gly Ser Leu Val Lys Ala Gly Ala Gly
 420 425 430

Ser Leu Val Leu Ser Gly Asp Ser Thr Tyr Arg Gly Pro Thr Leu Val
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30 Asp Gly Gly Leu Leu Ser Val Asp Gly Ser Leu Leu Ser Ala Val Glu
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35 Val Asn Ala Gly Gly Thr Leu Gly Gly Ser Gly Arg Ile Gly Gly Leu
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 485 490 495

45 Leu Glu Val Ala Gly Asp Leu Arg Phe Glu Ser Gly Ser Thr Tyr Ala
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Val Glu Leu Ser Glu Ser Ala Ser Asp Arg Ile Val Ala Ser Gly Lys
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50 Ala Ser Ile Ala Gly Gly Asn Val Thr Leu Ala Met Glu Asn Ser Pro
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Asp Leu Leu Ser Gln Ser Gln Val Glu Ser Leu Val Gly Arg Arg Tyr
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55 Asp Ile Leu Asp Ala Ala Gly Gly Ile Asp Gly Arg Phe Asp Ala Val

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55	Val	Ala	Gly	Tyr	Ser	Asn	Ser	Ser	Leu	Asn	Met	Asp	Ser	Ser	Leu	Gln
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		785					790					795				800
75	Gln	Lys	Ala	Lys	Leu	Asp	Ala	Gln	Ser	Ser	Gln	Leu	Phe	Ala	Glu	Ala
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Ala Tyr Ala Leu Gly Trp Arg Ser Leu Glu Leu Glu Pro Phe Ala Gly
820 825 830

5 Leu Ala Tyr Val His Val Ala Ser Asp Asp Phe Arg Glu Arg Gly Ser
835 840 845

10 Ala Ala Ala Leu Glu Gly Gly Asp Asp Asn Leu Asp Ala Ala Phe Thr
850 855 860

15 Thr Leu Gly Leu Arg Ala Lys Arg His Phe Glu Leu Asp Ala Gly Arg
865 870 875 880

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Claims

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- 55
1. An immunogenic composition comprising a PSE21-5 (PA5112) antigen and optionally one or more antigens selected from the list of: a PSE44-4 (PA3526) antigen; a PSE10-1 (PA1178) antigen; a PSE54 (PA5340) antigen; a PSE27-1 (PA0328) antigen; a PSE52-1 (PA4765) antigen; a PSE53-1 (PA5047) antigen; PSE11-3 (PA1248) antigen; a PSE41-5 (PA2407) antigen; a PSE47A-2 (PA4082); PSE5-1 (PA0595); PSE13-2 (PA1954); PSE17-1 (PA3692); PSE18-2 (PA4370); PSE20-1 (PA4735); PSE23-1 (PA3647); PSE24-1 (PA0126); PSE25-1 (PA0189); PSE26-1 (PA0274); PSE28-2 (PA0537); PSE31-2 (PA0737); PSE33-2 (PA1086); PSE42-1 (PA2793); PSE45-2 (PA3535); PSE50-1 (PA4578); PSE51-4 (PA4667); PSE19-1 (PA4710); PSE34-1 (PA1106); PSE36-3 (PA1324); PSE38-1 (PA1777).
 2. The composition of claim 1, comprising a PSE21-5 (PA5112) antigen in combination with at least one other antigen selected from the list: a PSE44-4 (PA3526) antigen; a PSE10-1 (PA1178) antigen; a PSE54 (PA5340) antigen; a PSE27-1 (PA0328) antigen; a PSE52-1 (PA4765) antigen; a PSE53-1 (PA5047) antigen; PSE11-3 (PA1248) antigen; a PSE41 (PA2407) antigen; a PSE47A-2 (PA4082); PSE5-1 (PA0595); PSE13-2 (PA1954); PSE17-1 (PA3692); PSE18-2 (PA4370); PSE20-1 (PA4735); PSE23-1 (PA3647); PSE24-1 (PA0126); PSE25-1 (PA0189); PSE26-1 (PA0274); PSE28-2 (PA0537); PSE31-2 (PA0737); PSE33-2 (PA1086); PSE42-1 (PA2793); PSE45-2 (PA3535); PSE50-1 (PA4578); PSE51-4 (PA4667); PSE19-1 (PA4710); PSE34-1 (PA1106); PSE36-3 (PA1324); PSE38-1 (PA1777).
 3. The composition according to claim 2, further comprising one or more antigens selected from the list: PilA, OprF-OprI, FliC, FliD, ExoA.
 4. The composition of claim 2, comprising at least one antigen selected from: PSE10-1 (PA1178), PSE52-1 (PA4765), PSE53-1 (PA5047) and PSE54 (PA5340).
 5. The composition of claim 2, comprising one or more antigens selected from the group consisting of: a PSE54 (PA5340) antigen; a PSE10-1 (PA1178) antigen; a PSE44-4 (PA3526) antigen; a PSE52-1 (PA4765) antigen; a PSE53-1 (PA5047) antigen; a PSE27-1 (PA0328) antigen; a PSE47A-2 (PA4082) antigen; or OprF-OprI.
 6. The composition of any preceding claim, wherein one or more of said antigens is adsorbed to an aluminium hydroxide adjuvant, and optionally wherein the composition includes a histidine buffer.
 7. The composition of any preceding claim, further comprising: one or more conjugates of (i) a *P. aeruginosa* exopolysaccharide and (ii) a carrier protein.
 8. An immunogenic composition comprising the composition of any preceding claim, and further comprising one or more of:
 - (A) one or more conjugates of a *S. aureus* exopolysaccharide;
 - (B) one or more protein antigens of a *S. aureus*;
 - (C) one or more pathogenic *E. coli* antigen/s; or
 - (D) one or more pathogenic *B. cenocepacia* antigen/s.
 9. An immunogenic composition comprising the composition of claim 1 and one or more of (i) a OprF-OprI antigen; (ii) a FliC antigen; (iii) a FliD antigen; and/or (iv) a PilA antigen.
 10. The composition according to claim 9 wherein the one or more antigens is a OprF-OprI antigen.
 11. The composition of any preceding claim, including an adjuvant.

12. A pharmaceutical composition comprising:

(a) a polypeptide comprising an amino acid sequence having 80% or more identity to SEQ ID NO: 3 which can elicit an antibody that recognises SEQ ID NO: 3; or

(b) a polypeptide comprising amino acid sequence SEQ ID NO:38; and

optionally further comprising an amino acid sequence having 80% or more identity to any one of SEQ ID NOs: 1-2, 4-35 or SEQ ID NOs: 36-65.

13. The immunogenic composition of any one of claims 1-11, for use:

(i) in raising an immune response against *Pseudomonas aeruginosa* infections in a mammal; or

(ii) as a prophylactic or therapeutic vaccine against nosocomial infections caused by *Pseudomonas aeruginosa*.



EUROPEAN SEARCH REPORT

Application Number
EP 17 20 1384

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DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	DATABASE Geneseq [Online] 15 June 2007 (2007-06-15), "Pseudomonas aeruginosa esterase, estA.", XP002781136, retrieved from EBI accession no. GSP:ADZ79322 Database accession no. ADZ79322 * sequence *	1-13	INV. A61K39/104 A61P31/04 C07K14/21
X	----- VICTORIA L CAMPODÓNICO ET AL: "Evaluation of flagella and flagellin of Pseudomonas aeruginosa as vaccines", INFECTION AND IMMUNITY,, vol. 78, no. 2, 1 February 2010 (2010-02-01), pages 746-755, XP002719211, ISSN: 0019-9567, DOI: 10.1128/IAI.00806-09 [retrieved on 2009-12-07] * abstract * * page 747, column 1, last paragraph - column 2, paragraph 3 * * page 750, column 2, last paragraph - page 751 *	1-13	TECHNICAL FIELDS SEARCHED (IPC) A61K
X	----- SAWA T ET AL: "Active and passive immunisation with the Pseudomonas V antigen protects against type III intoxication and lung injury", NATURE MEDICINE, NATURE PUB. CO, NEW YORK, vol. 5, no. 4, 1 January 1999 (1999-01-01) , pages 392-398, XP002142838, ISSN: 1078-8956, DOI: 10.1038/7391 * abstract * * page 394, column 2, paragraph 1 * * page 397, column 2, last paragraph - page 398, column 1, paragraph 1 * * figure 3a *	1-13	
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 17 May 2018	Examiner Noë, Veerle
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

EPO FORM 1503 03/82 (P04/C01)

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